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CARDIO-OMENTOPEXY IN THE TREATMENT OF ANGINA PECTORIS*

Report of Two Cases

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CORONARY arteriosclerosis, with its major complication, coronary thrombosis, is one of the major causes of serious heart disease which all too frequently attacks men in the prime of life whose other organs are still intact and healthy. We neither understand the factors involved in the onset of this arteriosclerotic process nor can we control its progress. Furthermore, medical treatment for these cases is either of no value or at best but palliative. It is no wonder, then, that many have turned to surgery to seek some direct means for increasing the blood supply to the myocardium.

Any method, therefore, whose principle is the improvement of the coronary circulation by surgically establishing a new blood supply to it is worthy of serious consideration and trial. Such a principle has been evolved and carried out in this country by Beck[1] and in England by O'Shaughnessy[2]; and although the principle of surgical revascularization followed by both has been the same, each surgeon has used different methods. Beck has developed a new blood supply to the heart by grafting to it a portion of pectoral muscle, whereas O'Shaughnessy has utilized a pedicled omental graft. To discuss all the voluminous clinical and experimental data bearing on this subject is beyond the scope of this report, but certain studies may be cited.

It is of course well known that attempts have been made for many years to improve the lot of the patient suffering from angina pectoris by an indirect surgical approach to the problem. These efforts have not been attended by notable success, so that operations on the sympathetic nervous system, which were at first encouraging, have since been demonstrated to be of little permanent value, and have been largely abandoned. For the same reason total thyroidectomy, designed for a similar purpose, has fallen into disuse.

Of recent years the clinical importance of the collateral blood supply to the heart has been emphasized by Hudson, Moritz and Wearn.[3] From their work it would appear that coronary occlusion is compensated for by channels from the remainder of the coronary circulation as well as by collaterals from the mediastinal circulation. The latter circulation includes connections to the coronary circulation from the pericardiacophrenic artery and the anterior mediastinal, pericardial, bronchial and esophageal branches of the aorta.

As has been stated by O'Shaughnessy,[2] it is clear that in many cases this collateral circulation is insufficient and that an infarcted area in the myocardium may go on to rupture within a few days, or may form a cardiac aneurysm which will sooner or later rupture from necrosis. In other cases a badly crippled heart is the result of the myocardial ischemia.

In cases where death does not follow coronary occlusion within a short time, the necessity for a compensatory and sufficient circulation to the myocardium is obvious. Although Spalteholtz[4] has shown a rich anastomosis between the right and left coronary trees, Leriche[5] has demonstrated experimentally that the efficiency of the collateral supply from the coronary system is a direct function of the state of the systemic blood pressure. And, also in this connection, Mautz and Beck[6] have recently shown a considerable variation in the degree of intercoronary anastomosis in the normal heart.

Utilizing a new technic of injection and dis-

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section, Schlesinger[7] has recently shown that anastomoses develop readily whenever and wherever arteriosclerotic narrowing or occlusion causes obstruction in the coronary artery circulation. These anastomoses are localized to the regions where they are needed. He concludes, moreover, as a result of these studies: "The coronary arteries, in *normal* human hearts, even senile hearts, are true Cohnheim end arteries, without anastomotic connections; such anastomoses do not develop *pari passu* with increase in age."

As regards the collateral extracoronary sources of blood supply, it has long been known that pericardial adhesions may be effective in the conduction of such new channels to the heart. Thus, Beck, Tichy and Moritz,[8] who experimentally produced broad areas of adhesions between the heart and the pericardium of dogs, found that the animals were able subsequently to survive almost complete occlusion of both coronaries through the use of silver bands. In man there is also convincing evidence which tends to corroborate the fact that visceroparietal pericardial adhesions efficiently aid the circulation to the heart. The formation of such adhesions in a given case of coronary occlusion, however, would seem to be a purely fortuitous circumstance. This is borne out by the autopsies on 83 cases of coronary occlusion reported by Parkinson and Bedford,[9] in which there were but 11 cases of pericarditis. Injection studies by Hudson, Moritz and Wearn[3] demonstrated the vascular connection between myocardium and pericardium when such adhesions existed.

From the foregoing experimental and other data, then, it would seem that if the heart muscle is to survive in some cases of coronary occlusion, sooner or later a rich blood supply, in the form of a collateral circulation, must become available to the myocardium. We have seen that such a compensatory circulation may form in the natural history of the disease. Indeed, as has been stated by Hochrein[10]: "We have learned to recognize that pericarditis is not a complication of coronary thrombosis but a natural attempt at healing — its presence is to be welcomed rather than deplored."

When adhesions do not form as a natural sequence, and when there is myocardial impairment as manifested by symptoms of cardiac ischemia, it would be desirable if the theoretical possibility of establishing such adhesions, and thereby improving the collateral circulation, could be brought to a practical clinical application. This has been effected by surgeons in this country and in Europe.

To Beck must go the credit for being the first surgeon to make an attempt at revascularization of the ischemic heart in the human subject. He had observed that adhesions were capable of carrying blood to the human heart when he divided such adhesions at operation and found that they bled profusely. He was also familiar with the published data of cases where death was due to other causes, in which the heart was found to have both coronaries completely occluded and pericardial adhesions were present. As a result of these and other experimental observations, Beck, using the pectoralis major muscle as a pedicled graft, attempted to bring a new blood supply to the heart in a human subject. In this he was notably successful, his first patient, a totally incapacitated farmer, operated on in February, 1935, being able to return to physical labor, free of pain, after a suitable postoperative period.

At the same time, in London, O'Shaughnessy was proceeding with experiments on cardiac grafting. Instead of muscle he used a pedicled omental graft. It has long been recognized that the omentum is the only structure in the body with the specific property of vascularization, and as a result of his accumulated experimental evidence as to the vascularizing power of the cardio-omental graft, O'Shaughnessy was convinced of its superiority over other structures available for the same purpose. Beck had also used the omentum as a graft in experimental animals.

In 1936 O'Shaughnessy published the results of a series of omental grafts in the racing greyhound. In the paper he showed that greyhounds which had previously been subjected to ligation of the left coronary artery and to a cardio-omentopexy were able to chase the electric hare around a full course (526 yards) without distress. By injection methods he demonstrated conclusively the vascular connections between the grafts and the coronary trees of the animals. Grossly, these were manifested by the appearance of the injection mass at the orifices of the coronary arteries when the sole vascular attachment to the heart was the omental graft through which the injection was made. Histologically, the new vessels were shown to extend to the deeper branches of the coronary artery, even under the endocardium.

In 1938 O'Shaughnessy reported on 20 human cases. In this series the patients selected for operation showed what he considered to be unequivocal evidence of cardiac ischemia and had failed to benefit by medical treatment. Fifteen of these patients were suffering from angina pectoris, and of these 10 received cardio-omentopexy, 3 pericardiotomy with insertion of an irritant (aleuronat), 1 cardiopneumonopexy, and 1 died on the table before the operation was fairly begun. There

were 5 deaths, only 1 of which was the direct result of operation. The other 4 occurred two months or more after operation as a result of uremia, pulmonary infarct, pneumonia and empyema, and "no apparent cause," respectively. Of the 10 patients who survived, 8 enjoyed freedom from angina, and 7 of the latter returned to work.

O'Shaughnessy has thought that the control of postoperative shock is an easier matter following cardio-omentopexy than following Beck's operation, because of the extensive dissection of the pectoral muscles which is a necessary preliminary to the latter procedure. Moreover, the operation is less time-consuming, and, other factors being equal, the omentum is obviously a better vascularizing agent than is the pectoralis major muscle.

Because of these various considerations, we have concluded that cardio-omentopexy, when feasible, is the operation of choice for the establishment of a new blood supply to the heart by surgical means. We have performed it in the two cases to be reported.

Selection of Cases for Operation

As may have been gathered from the foregoing discussion, no hard and fast indications for the selection of cases for operation have as yet been outlined. The final decision as to suitability for operation must rest with the cardiologist. From the surgeon's viewpoint, patients with angina are notoriously bad risks for operation by virtue of the very condition for which it is to be performed. This aspect, therefore, is a constant when arriving at a decision.

Other than this, however, we have insisted upon the fulfillment of several requirements. In so far as it is possible to determine, there must be, first, indisputable evidence of coronary heart disease with angina pectoris. Strict observance of this rule will, we believe, supply the necessary base line for the evaluation of the operation as a therapeutic measure. We insist, at present, that the patient be under sixty years of age and not obese. Serious complications in other organs are, of course, contraindications. We have rejected, and will continue to reject, patients with marked hypertension and cardiac enlargement.

If the patient fulfills the foregoing requirements, he is observed during a control period of one month, during which time exercise-tolerance and other tests are made.

We also are of the opinion that patients who give evidence of congestive failure are not suitable candidates for operation. Beck operated on a man in failure. He simply performed pericardiotomy by the removal of a cartilage under local anesthesia and introduced powdered beef bone for the purpose of increasing intercoronary communications or adding new capillary anastomoses from the pericardial fat. This patient stood the operation, but remained in failure and died four months later. Apparently the operation did nothing, one way or the other. We agree with Beck that the patient with coronary disease who is in failure is not a suitable person for operation.

With these patients the problem of weighing the immediate risk of operation against the prognosis without operation is a particularly difficult one. This is due to the fact that, as yet, time and the number of cases have not permitted an imposing array of figures from which to draw conclusions, and also to our inability to offer on the basis of the evidence at hand a sound prognosis in the absence of operation.

O'Shaughnessy has enlarged the scope of his indications to include 5 cases of non-anginal cardiac ischemia, but at the time of reporting, the operations had been too recently performed for conclusions to be drawn. There was 1 death, and 1 patient was able to return to work.

At the present time O'Shaughnessy[11] believes that cardio-omentopexy is relatively safe in the following circumstances:

A lapse of about six months after an attack of coronary thrombosis in patients with a clear previous history who are aged forty-five to fifty-five.

Specific aortitis with angina, provided the heart is not enlarged to any great extent.

Hypertensive heart failure, with the same proviso.

However, at least for a time, we prefer to confine ourselves to the narrower indications given earlier and limit our operations to patients having unrelievable angina pectoris.

Technic of Operation

Our procedure has been as follows when operation is decided on. For several days prior to operation the patient receives 3 gr. of quinidine sulfate three times daily, in order to reduce the irritability of the heart. Morphine sulfate is given in suitable doses preoperatively. After induction of anesthesia with ether vapor and oxygen, an intratracheal tube is introduced and connected to the anesthesia machine, in a closed system, so that differential pressure may be used.

The patient is placed in the dorsal recumbent position and an incision is made over the fifth left intercostal space extending from the mid-sternal line to the anterior axillary line. The left pleural cavity is entered through the fifth interspace, and after the fifth and sixth cartilages have been divided at the chondrosternal junctions

(Fig. 1) the Sauerbruch rib-spreader is placed. The left lung, if free of adhesions, will drop posteriorly as it collapses and allow an ample view of the pericardium (Fig. 2).

The phrenic nerve is identified on the pericardium and crushed lightly for the width of a

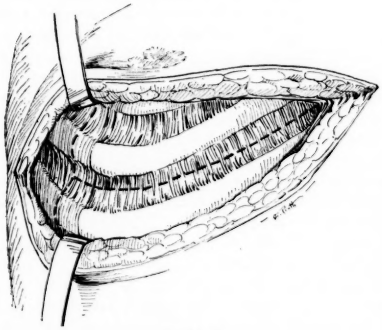

FIGURE 1.

This drawing illustrates the line of incision in the fifth left intercostal space. The cartilages are divided close to the sternum.

hemostat. This causes the left hemidiaphragm to rise into view (Fig. 2).

An opening is then made through the diaphragm in the direction of its fibers reasonably close to the pericardium and 5 cm. long. Through this opening the fingers deliver a suitable piece of omentum for attachment to the heart muscle. It is desirable that the omentum be pulled up until its lower margin can be obtained, and not grasped near the colon. Care must be used that undue tension on the transverse colon is avoided. The colon must not enter or encroach on the diaphragmatic opening (Fig. 3).

When sufficient omentum has been delivered through the diaphragm to cover the area of myocardium to be grafted, steps must be taken to close the diaphragm about the omentum and to prevent a later herniation of abdominal organs into the pleural cavity. In each of our cases we placed many interrupted silk sutures about the opening in the diaphragm in order to include the omentum and shut off the pleural cavity.

The pericardium is next opened (Fig. 3), and the omental graft is sutured to the heart muscle with interrupted silk sutures placed over its flat surface. The graft should be placed so as to overlap the branches of the right and left coronary vessels. Care must be taken to include no branches of the coronary vessels in the sutures. It is of great importance to avoid penetrating the entire wall of the ventricles.

When the omentum is widely covering the left lateral aspect of the ventricles, its edges are sutured to the cut edges of the pericardium and also to the inferior pericardiosternal ligament (Fig. 4).

The lung is next reinflated and the wound in the chest wall is closed in layers in the usual air-tight manner, employing interrupted perichondral

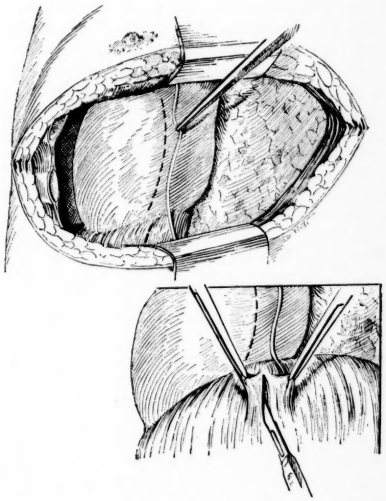

FIGURE 2.

In this drawing the ribs have been retracted and the lung has fallen backward, exposing the pericardium. The phrenic nerve is being pinched as it lies on the pericardium. The dotted line indicates the incision to be made in the pericardium and the direction of the incision in the diaphragm. The insert shows the diaphragm being incised, when it has risen into view after paralysis of the left phrenic nerve.

braided-silk sutures. At the conclusion of the operation, as in any intrathoracic procedure, it has been our practice to insert a needle and withdraw any trapped residual air from the pleural cavity, thus adjusting the inspiratory and expiratory pressures to their normal negative levels.

POSTOPERATIVE COURSE

The postoperative course has been remarkably uneventful in our two cases. We believe it important to maintain the blood pressure at a constant optimum level, in order to prevent stagnation and thrombosis in the coronary circuit, and to that

end the pressure is observed at very frequent intervals (every five to fifteen minutes) during the immediate postoperative hours. If the pressure shows any tendency to fall, 0.2 cc. of 1:1000 adrenalin solution is administered hypodermically. Quinidine sulfate is continued by mouth.

The pulse is usually paradoxical for a few days, and there may be irregularities of varying degree. Continuous nasal oxygen is administered, and the water balance is maintained by proper amounts of suitable fluids given parenterally. Fluid may accumulate in the chest, and if embarrassing to the patient may be removed.

Complications

In our first case, diaphragmatic hernia, from which acute obstructive symptoms arose, necessitating operative intervention, occurred six months after cardio-omentopexy and resulted in death. O'Shaughnessy[11] states that this complication has never been observed in any of his experimental animals, but that a hernia was found at autopsy in a case in which grafting had been performed two years previously. The patient, a woman, had died from chronic alcoholism with neurological and psychological symptoms, but apparently the diaphragmatic hernia had never given trouble. In our case the fundus of the stomach was incarcerated, and the patient was having bloody vomitus when he re-entered the hospital. The hernia was reduced and repaired by the abdominal route, but the patient died forty-five minutes after his return to the ward.

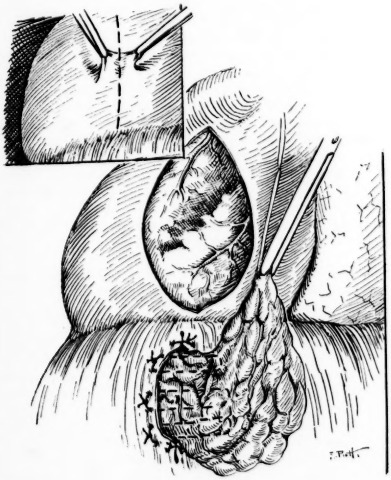

Figure 3.

The insert shows the incision in the pericardium. Usually the tense pericardium retracts markedly, thus exposing the heart. A suitable portion of omentum has been drawn through the diaphragm into the thorax. The dotted lines indicate the mattress sutures from side to side in the diaphragmatic incision through the substance of the omentum. The ends of the incision in the diaphragm have been sutured to bring it snugly about the omentum.

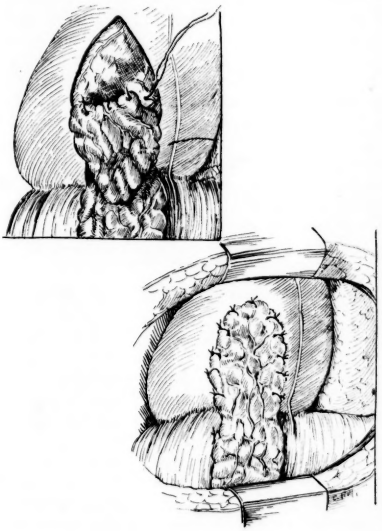

Figure 4.

The insert shows the surface of the omentum being sutured to the myocardium with multiple silk sutures, avoiding the branches of the coronary vessels. The lower drawing shows the suturing of the graft to the myocardium completed. Note the cut edges of the pericardium sutured to the omental graft in order to encourage further vascular anastomosis.

Certainly the technic of this operation must be seriously concerned with the prevention of postoperative diaphragmatic hernia, as well as with the attachment of omentum to the heart. We intend to do two things in the future to prevent such herniation. First, we shall do more careful suturing of the omentum to the diaphragm and of the ends of the incision in the diaphragm, since it seemed to us that in our first case the hernia opening in the diaphragm at autopsy was much larger than the original incision. Second, we in-

tend to run several crisscross silk sutures through the substance of the omentum placed in such a way as to include the sides of the opening in the diaphragm (Fig. 3). We shall not tie these sutures tightly enough to embarrass the circulation in the omentum. We expect that their presence will prevent herniation through the diaphragm.

In spite of presumably ample preoperative medication, the excitement and apprehension effected by bringing the second patient to the operating floor precipitated a severe attack of angina pectoris. Because of this it was necessary to postpone the operation for a week. The patient was not informed of the date set for operation; he was given Avertin by rectum in bed and brought to the operating room unconscious, after the manner of a "thyroid steal." The operation was performed without incident.

Results of Operation

O'Shaughnessy has now done fifty grafts but states that he will make no statistical analysis until he has done one hundred. His last reported series has been previously mentioned.

Beck, using pectoral muscle grafts, has operated on 25 patients. Of these, 16 are living and 9 are dead. The mortality rate in the first 12 cases was 50 per cent, and in the last 13, 15 per cent. Thirteen patients were observed for five months or longer after operation. There were no patients who were not improved by operation. Three had no pain, required no medication and had definitely increased exercise tolerance. Nine had pain, which was less severe, and took occasional medication, and the exercise tolerance was increased. One had some relief of pain and a slight increase in exercise tolerance.

In our two cases, whose histories follow, there was no operative mortality. The first patient died six months after cardio-omentopexy as a result of the repair of the diaphragmatic hernia. Following the primary operation he had had great relief from pain, required no drugs and showed a marked improvement in exercise tolerance.

The second patient has now lived for thirteen months since operation. He still has pain, which is less severe, requires some medication and has a greatly improved exercise tolerance. O'Shaughnessy states that improvement may be expected for twelve to eighteen months after operation.

Case Reports

Case 1. C. W., a 44-year-old, Swedish salesman, was admitted to the Evans Memorial on May 18, 1938. For the previous 2 years he had had substernal pain and oppression. During the last 6 months he had noted that less and less exertion produced the pain, so that eventually he could not walk across the street without having any. The electrocardiogram showed changes consistent with coronary heart disease, and there was suggestive evidence of an old infarction. The patient was transferred to the Division of Thoracic Surgery and on June 8, cardio-omentopexy was performed, uneventfully. The postoperative period was remarkably smooth and he was returned to the Evans Memorial for further medical observation on June 30. He was gradually allowed activity and was discharged to his home July 30.

From this time onward there was a progressive improvement in the exercise tolerance, so that about September 1, the patient was able to return to part-time work. He had some pain, but it was minimal, and a great deal more effort was required to bring it on. He boasted about his "new heart" to his friends. About October 1, he first noted discomfort after eating. About December 1, he had fullness in the left upper quadrant after every meal, with cramp-like pain radiating through to the left scapular region. He re-entered the hospital December 25 with evidence of acute gastric distress, vomiting some bloody mucus. It seemed evident that he had high obstruction, probably due to herniation through the diaphragm.

After suitable preparation, the patient was operated on December 28. A laparotomy was performed and the proximal third of the stomach was found herniated through the hiatus created by the cardio-omentopexy. This was repaired easily and the patient was returned to the ward in good condition. He died suddenly 45 minutes after his return to bed.

Autopsy was performed by Dr. Charles Branch. Microscopical study of sections at the site of the graft showed a rich capillary growth from it into the myocardium. There was extensive fibrosis of the myocardium, with multiple areas of old infarction.

Case 2. J. K., a 53-year-old, Lithuanian, Jewish shoemaker, was admitted to the Evans Memorial on October 15, 1938. For approximately 1 year prior to entry he had been suffering from typical attacks of angina pectoris. He experienced some relief of his pain with nitroglycerin and medical measures until March, 1938, when he had an attack lasting for 15 minutes. Since that time the attacks had been more frequent and the pain had developed on less and less exertion. The electrocardiogram was typical of coronary heart disease and the exercise-tolerance test was low. The patient continued to have attacks of anginal pain of varying degree while in bed under observation.

The patient was accepted for cardio-omentopexy and was brought to the operating floor on November 6. However, excitement and apprehension precipitated an attack of paroxysmal auricular tachycardia with a resulting status anginosus, and the operation was postponed. On November 15, Avertin was instilled into the rectum while the patient was still in bed on the ward. He was then brought to the operating-room and cardio-omentopexy was performed without incident.

Other than for some urinary retention, requiring constant drainage for a week, the postoperative period was entirely uneventful. The patient was transferred back to the Evans Memorial on December 5, and was discharged to his home, greatly improved, January 28, 1939.

He was last seen in November, 1939, at which time, he was improved as to exercise tolerance and as to the amount and frequency of his pain, and had returned to part-time work.

Summary and Conclusions

The experimental and clinical basis for attempting revascularization of the ischemic heart is briefly considered.

The indications for and technic of cardio-omentopexy are presented, and the complications discussed.

Two cases in which cardio-omentopexy was performed are reported.

Many more patients must be operated on before any sweeping conclusions may be drawn, but on the basis of the work already done we are encouraged to believe that the principle of revascularization is sound. At the present time, we believe that we should be concerned with establishing the fact that an adequate blood supply can be brought to the heart, regardless of the method used. When this has been definitely shown to be possible and physiologically efficient in the human subject, the method will become important.

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ACUTE PANCREATIC NECROSIS*

A Clinical Lecture

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I WISH to discuss a very interesting disease and to point out the advances made during the past decade in its diagnosis and treatment. I refer to acute pancreatic necrosis. I once heard Dr. Osler say that in presenting the subject of a particular disease to students it is always well to take an actual case as a text. Through the kindness of Dr. Putnam Kennedy, of the Boston City Hospital, I am able to follow this advice as I have before me the records of an instructive case which was studied there only a few weeks ago, and which through the courtesy of Dr. Soma Weiss I have permission to report. It illustrates most satisfactorily the newer knowledge in diagnosis and treatment.

Case Report

The patient, a 43-year-old woman, was admitted last October, suffering from bronchial asthma, a pulmonary infarct and phlebitis of the left saphenous vein. During the latter part of her hospital stay she complained mildly of vague gas pains in the epigastrium. She was discharged in early November but readmitted on November 12, in a state of shock. The previous night she had felt sudden, severe pain in the midepigastrium, followed by continuous vomiting of colorless, thin fluid. Pain continued throughout the night, increasing in severity, and in the morning the vomiting became more severe. Pain radiated from the midepigastrium into both upper quadrants and later involved the entire abdomen and the midback. The patient was brought to the hospital in an ambulance and when seen on the admitting floor was apparently in extremis. She was well oriented and able to recognize her surroundings, but rapidly became pulseless, with an audible heart rate of about 80. On two occasions she stopped breathing, but recovered after coramin and 50 per cent glucose had been administered intravenously.

Shortly after admission the pain extended to the cardiac area and to both shoulders. At physical examination the abdominal wall was thin and lax. There was no muscle spasm but great tenderness over the entire abdomen, especially in the upper quadrants, where it was more marked on the right than on the left. The rebound tenderness was most marked in the right upper quadrant. There was also tenderness over both shoulders. At 9 p.m. the temperature was 97.6°F., the respirations 28, and the pulse 70. The leukocyte count was 18,400. The urine was free from albumin and sugar, and contained bile but no urobilinogen. The diagnosis on admission was "acute surgical abdomen," due either to a ruptured gall bladder or to acute pancreatic necrosis.

The following day, November 13, the temperature was subnormal. The urine still contained considerable bile. The urinary diastase was 256 units (Fig. 1). Dr. Stanley J. G. Nowak saw the case in consultation and noted tender-

*Delivered at the first meeting in the auditorium of the Joseph H. Pratt Diagnostic Hospital, December 6, 1938.

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ness in both flanks, especially in the left over the tail of the pancreas. This, together with the afebrile response, the presence of bile in the urine and the improvement with conservative treatment, led him to make the diagnosis of acute pancreatitis. Dr. Irving J. Walker agreed with this diagnosis, as did Dr. Weiss, who noted maximum pain in the upper abdomen, particularly to the left just below the costal margin. On November 14 the urinary diastase fell to 64 units, which is the upper limit of normal. The icteric index was 5. The temperature rose to 100.6°F. (axilla), and the pulse to 104. There was a trace of bile in the urine. After this date, bile was no longer present, but urobilinogen, first noted November 13, was found in increasing amounts until November 20. On November 16 there was still tenderness over the entire upper abdomen and in both flanks. The following day fluid was given

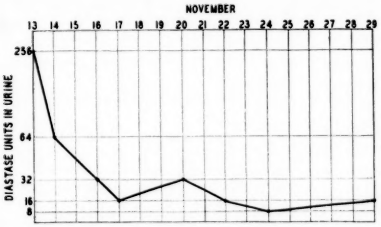

FIGURE 1.

by mouth for the first time since admission, beginning with 1 teaspoonful of water every hour. The fasting blood sugar was determined for the first time that day and was 70 mg. per 100 cc. The patient made a good recovery.

SYMPTOMS AND SIGNS

The first and most important symptom of acute pancreatic necrosis is pain. It is severe, often agonizing, not colicky but continuous and usually unrelieved by morphine. Moynihan[1] asserts that the pain is the most severe type of any resulting from abdominal disease and is attended with the most profound collapse. The location of the pain is significant. It is in the upper abdomen, usually in the epigastrium. Sometimes, as in the case reported, it extends across the entire front of the abdomen. It often radiates to the left back and occasionally, as here, to the midback. Brocq[2] maintains that the extension of the area of pain across the abdomen is an indication of an involvement of the entire pancreas; if the necrosis is confined to the head of the pancreas, the pain is to the right of the midline.

Vomiting accompanies the pain in almost all cases. This patient vomited repeatedly. When there is a great deal of hemorrhage into the pancreas, some blood may pass from the pancreatic duct into the duodenum and appear in the vomitus. Usually, however, as in this case, there is nothing distinctive in the character of the vomitus. On inspection the patient appears very ill. Sometimes there is cyanosis of the lips. There is a striking contrast between the severity of the condition and the scarcity of objective findings. At onset the temperature is normal and the pulse, although weak, may be little if at all accelerated. In a day or two moderate fever develops. There is tenderness in the epigastrium but no muscle spasm as a rule. A soft abdomen which permits deep palpation is characteristic. The location of the tenderness is often an aid in the diagnosis of acute pancreatic necrosis. The late Daniel F. Jones,[3] one of our ablest diagnosticians, whose opinions were based on an unusually great experience with acute pancreatic necrosis, held that the most satisfactory aid in making the diagnosis was the careful determination of the location of tenderness. He wrote:

> It is not enough to say there is tenderness in the upper abdomen. Given symptoms suggesting gall-bladder disease, the diagnosis of pancreatitis should be made correctly in a high percentage of cases if there is tenderness extending to the left from the gall bladder. This can be accomplished only by meticulous care as to the amount and extent of the tenderness. Experience is necessary, of course, to make this distinction, and yet a former resident, of very moderate hospital experience, made a correct diagnosis in the next two cases that were admitted after he had been taught this method of diagnosis.

The clinical picture of what Dieulafoy[4] calls *le drame pancréatique* has been drawn by many writers in different countries, and there is a striking similarity in their descriptions. An obese person of middle age addicted to alcohol and with a history suggesting cholelithiasis is suddenly seized shortly after a heavy meal with agonizing pain in the epigastrium, accompanied by vomiting. The pain continues, unrelieved by morphine, and vomiting persists. Signs of collapse appear. The temperature and pulse are not elevated. Aside from epigastric tenderness nothing of significance is found on examination of the abdomen. Symptoms continue many hours without abating.

Until the introduction of the diastase test the correct diagnosis was usually made at operation or autopsy. In a series of 121 cases analyzed by Brocq,[2] the diagnosis of acute pancreatic necrosis was made in only 21. It was most commonly mistaken for perforation of a peptic ulcer (25 cases),

for ileus (23 cases), for peritonitis (15 cases), for appendicitis (13 cases) and for cholecystitis (11 cases). One physician mistook the case we have discussed for a rupture of the gall bladder. All the others of the staff made the correct diagnosis at their first examination. If, as stated, the symptoms of acute pancreatic necrosis are characteristic, it is a fair question to ask, Why is the diagnosis usually missed? The chief reason is that owing to its rarity it is not considered. Undoubtedly mild cases are often overlooked, and typical severe cases are certainly rare. Halsted, the distinguished Johns Hopkins surgeon, told Brown[5] that he was eager to make a preoperative diagnosis of acute pancreatitis before he died, but his wish was not gratified. He saw only 2 cases; in neither was pancreatic disease suspected, and in both the correct diagnosis was determined only by exploratory operation. Körte[6] said that surgeons fail to recognize the disease because they forget that every sick man has a pancreas. Garrod[7] expressed the same thought when he wrote: "The chief difficulty in diagnosing disease of the pancreas is in thinking of the pancreas."

Knowledge of etiologic factors should be an aid in diagnosis. The disease affects men and women about equally. There were 182 men and 150 women in Brocq's series. In the largest collection of cases assembled (Schmieden and Sebening[8]) 77 per cent of the patients were women. Most cases occur between the thirty-fifth and fifty-fifth years. The frequent association with biliary disease is undoubted. In some German clinics this is as high as 90 per cent. The percentage is much lower in some studies. Myers and Keefer[9] found only 10 cases of biliary disease among 48 cases of acute pancreatic necrosis collected from the records of the Mallory Institute of Pathology at the Boston City Hospital. Jones[3] found that 22 cases of acute pancreatic necrosis at the Massachusetts General Hospital occurred in patients without gallstones. In a review of 38 cases of acute pancreatic necrosis that came to autopsy at the New Haven Hospital (Weiner and Tennant[10]) there was extrahepatic disease in only 6, or 16 per cent. In 25 cases (66 per cent) alcoholism was an associated factor.

Pathology

Twenty years ago I[11] wrote in the section on diseases of the pancreas in *Oxford Medicine:*

> The severe, acute disease of the pancreas often called acute hemorrhagic pancreatitis is unlike that of any other organ, because the disease is due to the destructive action of the pancreatic juice on the very tissue that formed it and the general symptoms that occur result from the absorption of toxic bodies produced by this autodigestion.

Opie and Meakins[12] in 1909 used the term acute hemorrhagic necrosis, but acute pancreatic necrosis (Guleke[13]) or acute toxic necrosis of the pancreas seems preferable, as the lesion is not always hemorrhagic. Brocq[2] calls it *pancréatite aiguë aseptique* —a good term because it emphasizes the nonbacterial nature of the disease. As early as 1909 Opie and Meakins pointed out the essential fact that the disease is not an infection but an intoxication. This truth has gained acceptance slowly, and some surgeons even today still falsely call the disease an infection. Nordmann[14] emphasizes the importance of a knowledge of the pathology of the disease as a basis for correct ideas in regard to treatment. He says that so long as one speaks of pancreatitis and continues to regard the disease as one of inflammatory origin, and plans surgical procedures according to this conception, so long will he travel a false path. Autodigestion of the pancreas through activation of the pancreatic juice is the cause of the edema, necrosis and hemorrhages in the gland. Producing occlusion of the pancreatic ducts in dogs by ligatures applied with every aseptic precaution is followed by the speedy production of acute pancreatic necrosis in a large percentage of cases. This I know, since I have lost quite a number of dogs when the pancreatic ducts were tied for this purpose. These experiments disprove the theory that the introduction of infected material into the pancreatic ducts from the common bile duct is essential to the production of the disease, and they prove conclusively that trypsin can be formed readily within the gland from the inactive trypsinogen.

How the disease arises clinically remains a mystery. Many factors are probably concerned. The pancreatic duct is rarely found to be stained with bile at autopsy. Furthermore, the pressure in the duct is higher than that in the common duct during digestion, and pancreatic ferments have been recovered from the gall bladder in a considerable proportion of the cases examined. The common-channel theory of Opie explains very few cases. Many years ago Archibald[15] suggested that spasm of the sphincter of Oddi might lead to the entrance of bile into the pancreatic duct, with the resulting development of acute pancreatic necrosis, and supported his theory by experimental evidence. Wangensteen and his associates[16] have shown that by closing the sphincter of Oddi in cats by a ligature the stimulus furnished to the contractile mechanism of the gall bladder by a fat meal produced acute pancreatic necrosis in 15

out of 31 experiments. Only 2 of Weiner and Tennant's[10] 38 cases could be explained on the basis of the reflux theory. In 3 other cases in which they found a common channel the pancreas was normal. Inasmuch as the ferments may be activated within the gland, as we have shown experimentally, the theory of Rich and Duff[17] that the disease is due to occlusion of the smaller pancreatic ducts by a metaplasia of the duct epithelium is an attractive one. However, in a great majority of cases the pancreas, the seat of acute pancreatic necrosis, fails to show this metaplasia with the resulting occlusion. Nervous and circulatory changes in the pancreas may prove to be most important in the etiology of this disease, but it is futile to speculate concerning them.

Classification of Cases

The cases of acute pancreatic disease can be divided into three groups: acute pancreatic edema, acute pancreatic necrosis and suppurative pancreatitis. These will now be discussed.

Acute Pancreatic Edema

Since Zoepffel's[18] paper in 1922 this disease has been recognized with increasing frequency. It is probably the commonest form of pancreatic disease, and is often associated with cholelithiasis. In this country excellent studies of this condition have been made by Elman[19] and Cole.[20] The latter observed no less than 6 such cases in a series of 8 proved cases of acute pancreatic disease at the Illinois Research and Educational Hospital during a period of eighteen months. The symptoms are similar but of less intensity than those in acute pancreatic necrosis. Shock, according to Cole, is never encountered in this type of the disease. Acute pancreatic edema is frequently seen in association with gall-bladder disease, and the pain and vomiting are usually attributed to the accompanying cholelithiasis. There is a leukocytosis, but it is usually less than that in pancreatic necrosis. A high diastase value in the blood or urine is diagnostic of pancreatic involvement. Swelling and induration of the pancreas may be marked, and may involve either a portion or the whole of the gland. The condition is regarded as the earliest stage of acute pancreatic necrosis, but biopsies reveal only an interstitial edema. There is rarely any free fluid in the peritoneal cavity. There may be fat necrosis, as in 2 of Zoepffel's original cases, but if there are areas of necrosis in the gland the condition has passed into the second stage and should be classed as mild acute pancreatic necrosis. Recovery as a rule occurs in a few days.

Acute Pancreatic Necrosis

This has already been described in sufficient detail. The case presented is typical of the disease in its severe form. Some patients die within a few hours, and at autopsy the pancreas may be converted into a hemorrhagic mass. These deaths were formerly attributed to apoplexy of the pancreas. A considerable number of cases were reported with this diagnosis before Fitz[21] published his epoch-making lectures on acute pancreatitis in 1889. They were really fulminating cases of acute pancreatic necrosis in which the areas of necrosis were overlooked.

Suppurative Pancreatitis

To this group belong also the cases of true gangrene of the pancreas. Both conditions may occur secondary to acute pancreatic necrosis if bacteria lodge and grow in the necrotic tissue. They are rare sequelae. After initial improvement in a case of acute pancreatic necrosis the temperature increases and may be septic in type. The leukocytosis becomes more marked or develops for a second time and usually to a higher degree, the white-cell count sometimes reaching 30,000 or more. Pain and tenderness become localized, usually in the epigastrium or left loin. The physician should be alert to recognize this condition, as incision and drainage constitute the only treatment that will result in cure. If operation is delayed, general sepsis may occur. Suppurative pancreatitis with abscess formation is sometimes seen following the extension of a peptic ulcer into the pancreas, but this is rare. Bernhard[22] says that in a series of 200 cases of acute pancreatic disease he saw only 1 of bacterial infection.

Laboratory Aids to Diagnosis

Increased Diastase Values

The most important laboratory aid in the diagnosis of acute pancreatic disease is the determination of the diastase activity of the urine and blood. The test has been applied now in hundreds of cases, and its value in the diagnosis of acute interstitial edema of the pancreas and of acute pancreatic necrosis is undoubted. The method introduced by Wohlgemuth[23] in 1908 and modified by him[24] in 1929 is the one most satisfactory for clinical use, because it is so simple that it can be carried out by any intern or laboratory technician. A report can be rendered within an hour of the receipt of the specimen, so that the test may be utilized as an aid in the speedy diagnosis of acute abdominal conditions. More accurate methods of amylase determination are available, but they

are time-consuming and require more equipment and the services of a chemist. As only a great increase in amylase values is of diagnostic significance, the Wohlgemuth method is entirely satisfactory for the purpose.

In 1918 McClure and I[25] reported 4 cases of acute pancreatic necrosis in which all the diastase values in the urine were normal. We concluded at that time from our own experience and a study of 6 cases previously reported in the literature that the test was of very little value. The cause of our negative results is now clear. All the tests were performed relatively late in the course of the disease, one week or more after the diagnosis was made at operation. About ten years ago the important discovery was made that the diastase value usually falls to normal after the first two or three days. It may be elevated for only the first twenty-four hours. A fresh morning specimen of urine or the twenty-four-hour amount should be used for the test. If there is a delay in making the examination the urine should be covered with a layer of toluol. Blood should be collected in a dry test tube and allowed to clot. The serum is used for the test. If diastase determinations of the urine are made daily or every other day, valuable information is often obtained. The diastase activity of the urine should be at least 256 units to be of diagnostic value. If it is above this level it is a definite indication of pancreatic disease.

In the case we are studying the urine contained 256 units. Some authorities hold that this is not a sufficiently high value to incriminate the pancreas. It is regarded by all as the lower border of significant value. But note that in the case here reported the examination was not made until at least thirty-six hours after the onset. Fortunately, subsequent determinations were made which are most instructive. The following day, the diastase value was at the normal level, only 64 units being present. The course of the curve in the chart certainly suggests that if a diastase determination had been made when the patient was admitted it would have been at a higher level. The rapid fall in diastase furnishes as strong evidence as did the original level of 256 units that the patient had acute pancreatic necrosis. The diastase test is said to be negative even in the first twenty-four hours of the disease in from 10 to 20 per cent of cases. According to Doberer,[26] examination of the urine is preferable to that of the blood. In the cases he studied in Clairmont's clinic the blood diastase was normal in the majority of cases, although urinary diastase was almost always increased. Hence other tests are necessary in some cases.

Increase of Lipase in the Blood

In 1932, Cherry and Crandall[27] demonstrated that a lipase which hydrolizes olive oil, normally not present, appeared in the blood following the ligation of the pancreatic ducts of dogs. The activity of the enzyme, esterase, normally present in the blood as measured by hydrolysis of ethyl butyrate or tributyrin, did not show uniform increase in their experiments. They devised a simple titration method for the determination of lipase in the blood serum, using olive oil as a substrate. Comfort,[28] using this method, recently obtained elevated values in 20 of 21 cases of acute pancreatic necrosis examined within ten days after the onset of symptoms. The upper limit of lipase activity in persons without pancreatic disease is given by him as about 1.5 cc. in terms of N/20 sodium hydroxide per cubic centimeter of serum, although Cherry and Crandall found that the serums of 40 of 46 patients did not reveal any trace of lipase capable of splitting olive oil. In acute pancreatic necrosis a value as high as 10.2 cc. has been obtained. The earlier in the disease the blood was examined, the higher was the value. Fourteen days or more after onset the serum lipase was normal.

Leukocytosis

There is usually a marked increase in the leukocyte count, which often exceeds 25,000. It is sometimes as high as 50,000. In a case of acute pancreatic edema in my series, proved by operation, the leukocyte count was 27,000, although the temperature was only 98.6°F. In the present case the leukocytes on admission numbered 18,400. A rapid fall, as occurred during the first week, is a good prognostic sign.

Hyperglycemia

The fasting blood sugar is elevated in 50 per cent or more of cases, hence its importance in diagnosis should be stressed. Brocq and Varangot[29] found the blood sugar above 150 mg. per 100 cc. in 57 out of 72 cases, and in 34 of these it was above 200 mg. Recently Dunlop and Hunt[30] report that it was elevated in 6 out of 7 cases they studied, and in 5 of these to more than 200 mg. Even when the fasting level is normal a glucose-tolerance test may prove of value. Löffler,[31] using Staub's method, demonstrated the value of this procedure. In 5 cases of acute pancreatic necrosis the initial blood sugar was below 140 mg. and in 3 of these 110 mg. or less. Yet in all 5 cases an abnormal glucose-tolerance test was obtained. In 2 of these the blood-sugar level rose above 200 mg. in the second or third hour.

Other Aids to Diagnosis

Some writers hold that an increase of urobilinogen is of diagnostic value. Bernhard[32] found it increased in 11 out of 12 cases of acute pancreatic necrosis. In the present case there was a progressive rise during the first week, although it was absent at the first examination. Bile in the urine at onset was an aid in the diagnosis. A high serum bilirubin has been observed in some cases. The nonprotein nitrogen may be increased. It was above 40 mg. per cent in 14 out of 25 cases studied by Bernhard.[32] An x-ray film of the abdomen and lower chest may be of diagnostic value. Berg[33] maintains that meteorism of the stomach and transverse colon occurs with great regularity in acute pancreatic necrosis, as well as changes in the lower part of the duodenum. Shadows at the bases of the lungs may be due to pancreatic disease, as Röpra[34] has shown.

Treatment

The case described in this lecture was one of fulminating acute pancreatic necrosis. Many surgeons would have held that an operation offered the only hope of recovery. Drs. Walker and Nowak thought differently. They did not operate, yet the patient recovered. At the beginning of 1929 all surgical authorities were agreed that early operation was indicated, although early diagnosis and early operation had failed to reduce the high mortality, which remained between 50 and 60 per cent. In that year Pólya[35] offered the first protest against this procedure. In 1938 Nordmann,[14] in an excellent paper on the diagnosis and treatment of acute pancreatic necrosis, stated that the death rate among his patients had fallen from 50 to 24 per cent since conservative treatment had been followed. He gave other figures as follows: conservative treatment in Walzel's clinic resulted in a fall in death rate from 86 to 28 per cent; Bernhard's death rate fell to 7 per cent; Demel's fell from 78 to 28 per cent; and Haberer's from 54 to 23 per cent. In a discussion that followed the reading of Nordmann's paper all the surgeons present supported his views. Guleke,[36] the well-known authority on pancreatic disease, stated that of his 46 patients on whom operation was performed 12 died, a mortality of 26 per cent, while of 8 conservatively treated patients all recovered. Puhl[37] reported that under conservative treatment in the Kiel clinic the mortality fell from 45 to 7 per cent.

Some American statistics likewise show a lower mortality under conservative treatment. The experience at the Boston City Hospital is instructive. There the mortality rate has fallen from 54 per cent in cases submitted to early operation to 25 per cent under conservative measures (Lium[38]). Dr. Walker[39] stated his views in a recent discussion as follows:

> One can be sure that most edematous cases of pancreatitis, and some hemorrhagic ones, will recover spontaneously or by medical treatment. Practically it appears that if one suspects acute pancreatitis of low grade, as evidenced by symptoms and clinical findings, surgery is not advisable for the disease per se, but may be indicated on the basis of an accompanying acute lesion of the gall bladder. Likewise, emergency surgery is contraindicated in those cases of hemorrhagic pancreatitis where shock and toxemia are manifest. Under treatment consisting of parenteral fluids and decompression of the upper intestinal tract by the Wangensteen method, some of these cases will recover without surgery, and those in which surgery becomes necessary will be better prepared for it. The treatment of suppurative pancreatitis calls for no special comment, other than that the pancreas should be drained when pus is apparent.

The statistics just cited are additional evidence of the correctness of Dr. Walker's opinion that conservative treatment rather than operative procedures is indicated in dealing with acute pancreatic necrosis. With this view I am in accord. As the disease is not an infection but an intoxication in which trypsin and split-protein products are absorbed by the lymphatics and blood vessels of the pancreas, it would seem evident that this absorption cannot be prevented by any operation, but might on the other hand be increased by incising or even manipulating the pancreas.

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COMPARATIVE STUDY OF THE TUBERCULIN PATCH TEST AND THE STANDARD INTRADERMAL TEST (PURIFIED PROTEIN DERIVATIVE)

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FOLLOWING the introduction of the tuberculin patch test by Vollmer and Goldberger,[1] an attempt has been made to compare its value with the standard intradermal test used for several years by the New Hampshire Tuberculosis Association in its case-finding surveys. These surveys have consisted in the tuberculin testing of various groups of high-school students throughout the State, followed by an x-ray examination of the lungs of all the positive reactors. The standard intradermal test consists of 0.1 cc. first-strength Purified Protein Derivative, which corresponds to 0.1 cc. of a standard Old Tuberculin in the dilution of 1:10,000.

During 1938 we directed these case-finding surveys, and the tuberculin patch test was compared with the standard intradermal test in 1455 high-school pupils. Most of them were between twelve and sixteen years of age and hence in an age group that was deemed satisfactory for comparative testing. Both tests were made simultaneously on each child—the standard test intradermal on the left forearm and the patch test‡ on the right forearm. Before applying the patch test the skin was cleansed with ether or acetone. In order to obtain their fullest co-operation, the pupils were enlightened in detail at the first session as to the purpose of the tests and the conditions necessary for the most effective results.

The following rules were to be observed:

The patch-test area was to be kept absolutely dry.

If any portion of the adhesive became loosened it was to be immediately covered by a fresh piece, as perfect contact between the skin and the patch was desired.

The patch was not to be removed, even temporarily, by the subject for any reason without consent of the nurse.

The patch was to be removed by the nurse at the end of forty-eight hours; the test was to be read at that time, and again after another forty-eight hours.

Any reaction at the site of the patch test within one week after the second reading was to be reported.

The majority of the pupils showed a very helpful attitude after having the work explained to them. Table 1 gives the results obtained.

TABLE 1. *Results of Patch and Intradermal Tuberculin Tests.*

LOCATION OF HIGH SCHOOL	NO. OF PUPILS TESTED	NO. OF PUPILS POSITIVE TO BOTH TESTS	NO. OF PUPILS POSITIVE TO INTRADERMAL TEST ALONE	NO. OF PUPILS POSITIVE TO PATCH TEST ALONE	POSITIVE REACTORS TO ONE OR MORE TESTS %
Ashland	105	10	0	0	9.4
Charlestown	72	13	0	0	18.0
Claremont	238	52	9	0	25.6
Epping	81	13	0	0	16.0
Jaffrey	122	16	0	0	13.1
Penacook	93	10	0	0	10.7
Pittsfield	116	3	6	0	7.8
Lebanon	347	44	0	1	13.0
West Lebanon	85	10	0	1	12.9
Lincoln	79	7	0	1	10.1
Marlboro	117	24	0	0	20.4
Totals	1455	202	15	3	15.1

Most of the positive reactions with the patch

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‡The patch-testing outfits were supplied through the courtesy of the Lederle Laboratories, Incorporated, Pearl River, New York.

tests were sharply defined. Slight blistering was observed in the more pronounced reactions. It was noteworthy that in a few cases the patch test did not become positive until from five to seven days after the removal of the patch.

In practically all cases the patch-test results ran parallel with those of the intracutaneous test. The poor ones noted in the groups at Claremont and Pittsfield emphasize the importance of mechanical difficulties. Here alcohol was used in cleansing the arm in some instances, and a check-up showed that in nearly every case the adhesive had not stuck properly.

Judging from the results obtained, the patch test would seem to lend itself to large-scale group testing for the following reasons: reliability (it compares favorably with the standard intradermal test); ease of application (it may be applied rapidly even by an unskilled person, and there are no instruments to sterilize); acceptability (the fear of the needle in the minds of both the parents and the child is no small force in holding back a campaign for the skin-testing of large groups); and stability over long periods (since the tuberculin on the patches is in dry form, they may be kept indefinitely). Against the use of the patch test are the obvious mechanical difficulties which are intrinsic in the patch itself or due to lack of co-operation on the part of the subject. The former can be helped by an improvement in the quality of the adhesive plaster used, whereas education as to the value of the test will help to ensure the co-operation and interest of the child.

The patch test offers to the internist and pediatrician a simple, effective and acceptable means for the tuberculin testing of private patients. This fact and the adaptability of the method to group testing should give impetus to the worthy campaign, the eventual goal of which is the tuberculin testing of all citizens of the United States.

TABLE 2. *Results of X-Ray Examination of Positive Reactors.*

RESULTS	NO. OF CASES
Adult-type pulmonary tuberculosis	0
Healed tuberculous foci in lungs	2
Healed calcified tracheobronchial nodes	31
Soft calcified tracheobronchial nodes	9
No lesions (healed or active)	145
Total	187

It is interesting to note that 187 of the positive reactors received a follow-up x-ray examination of the lungs with the results shown in Table 2.

SUMMARY AND CONCLUSIONS

An attempt has been made to evaluate the use of the tuberculin patch test in comparison with that of the standard intradermal test now used in New Hampshire in tuberculosis case-finding surveys. The results tend to show that the patch test, because of its reliability, ease of application, general acceptability and stability, is equally satisfactory and should prove to be a useful method for case finding, not only in the testing of large groups but also in private practice.

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CAN INFANTILE PARALYSIS BE SPREAD BY BATHING IN SEWAGE-POLLUTED WATERS?

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INFANTILE paralysis, otherwise known as acute anterior poliomyelitis, has appeared in epidemic form in the United States at more or less regular intervals during the last thirty years. While epidemics were reported in Europe previous to 1907, this date marks the first serious one in the United States. Because of the nature of the disease and the effect on its victims, great interest has been aroused in its mode of transmission and the methods of controlling its spread.

Epidemiologists agree that infantile paralysis is commonly transmitted by direct contact. There also seems to be evidence that it is sometimes transmitted indirectly through a third person. It is held by some that contact infection is not the only way by which the disease is transmitted. Ever since the outbreak in 1907, each epidemic has suggested new possibilities as to agencies of transmission. Practically every conceivable agent which might carry the disease has been investigated during the last thirty years, but so far the chief value of these investigations has been only to disprove this or that theory.

In 1934 I was engaged to study the problem of sewage disposal at Fall River, Massachusetts. The sewage of that city is discharged without treatment through a number of outfall sewers into the waters of Mount Hope Bay, at the mouth of the Taunton River. During the course of the investigation it was necessary to study the tidal currents in this bay, partly to determine the effect of the discharge of sewage along the waterfront, and partly to aid in selecting a suitable location for an outfall sewer from a proposed sewage-treatment plant.

For the most part the waterfront at Fall River is devoted to commercial and industrial uses. At several points along it, however, there are beaches, two of which are used quite extensively for bathing. While the latter are at some distance from the most important outfall sewers, current observations showed that under certain conditions of wind and tide they were affected by sewage pollution. Many years ago sewage pollution in Mount Hope Bay became so serious that the taking of shellfish was restricted by the state health authorities, and, partly as a result of the Fall River sewerage investigation in 1934, the restricted area was extended well beyond the former limits.

In the summer of 1935 Massachusetts was visited by an epidemic of infantile paralysis, the incidence of which, according to the Massachusetts Department of Public Health, reached the third highest figure in the history of the State. Fall River, with 114 cases reported, had the highest incidence of any city or town. Having but recently observed the effect of sewage upon the bathing beaches at Fall River, I could not but wonder whether this pollution had any effect on the high incidence of infantile paralysis in that city. It has been shown experimentally that the virus of infantile paralysis can gain entrance into the central nervous system through the olfactory nerve endings, and there is considerable evidence that this avenue of infection, through the nasal mucosa, is quite common. If it were possible for sewage to carry a sufficient concentration of this virus, what better way would there be of producing a case of infantile paralysis than frequent flushing of the nasal passages with sewage-polluted water, as would be done in bathing, particularly by youngsters with a natural proclivity for diving and swimming under water?

This possibility was also suggested by the fact that the points of highest incidence in Massachusetts in 1935 seemed to be in communities bordering on waters used for bathing and affected by sewage pollution. A large number of cases were reported in the Boston Metropolitan District and in the communities bordering on Salem and Beverly harbors. In each of these districts there are many bathing beaches, some of which are known to be affected by sewage pollution. The cities and towns along the Merrimac River reported a high incidence of infantile paralysis in 1935. Sewage pollution along that river has for many years been a serious problem, although bathing in its polluted stretches is not common. The highest concentration of pollution occurs near Haverhill. In this connection a statement in the annual report of the Massachusetts Department of Public Health for 1917 appears to have some significance. In the section of the report concerning acute poliomyelitis in that year the following comment was made: "Cases were well distributed except in Haverhill, where 38 cases were reported

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from June to September. The disease has prevailed constantly in Haverhill for the past few years to a greater extent than in some other communities of the same size or larger."

Previous to 1912 it had been demonstrated that the virus of infantile paralysis could be recovered from the mucosa of the intestinal tract and from the feces.[1] Trask, Vignec and Paul[2] have recently reported on the recovery of the virus from the stools of an infant following an illness from abortive poliomyelitis. Emulsions prepared from the stools on the second, fourteenth and twenty-fifth days following the onset of the disease were used to inoculate monkeys. In each case paralysis developed seven days after inoculation. As evidence of the resistance of the virus, one of the stool samples was kept under refrigeration for ten weeks and the virus remained viable for this length of time. According to the authors, such facts suggest that, during an epidemic, unrecognized forms of the disease may be responsible for a high degree of pollution of sewage with poliomyelitis virus.

Lovett and Richardson[3] as far back as 1911 suggested that the disease seemed to prefer river valleys, but concluded that this was probably because of the increased opportunities for personal contact, since highways and railroads frequently follow such valleys. They reported, however, that of 419 cases from 1908 to 1910, 105 cases, or slightly more than 25 per cent, showed a history of swimming, wading or paddling in more or less contaminated water just prior to the attack. However, these authors called attention to 457 cases during the same period, 34 per cent of which showed a history of having been preceded by accidents, overexertion or falls, and concluded that there was at least as much significance in the effect of accidents as in the effect of bathing in contaminated water. If the cases studied by Lovett and Richardson followed the usual age distribution, it is obvious that a relatively large number of children in the first-mentioned 419 cases would have been too young either to bathe or to paddle. Excluding the very young children, the proportion of cases showing a history of bathing in contaminated water would have been substantially greater than 25 per cent. With the evidence gathered by Lovett and Richardson it may seem strange that they gave this factor so little weight; it should be remembered, however, that little was known regarding the disease in 1911 as compared with what is known today. The following statement in their treatise is significant: "There is nothing in the pathologic anatomy and histology of the disease which shows the mode of entrance of the infectious agent into the body nor whether it reaches the central nervous system by the blood or by the lymph stream."

It is generally held that infection by poliomyelitis is much more widespread than would be indicated by the number of cases diagnosed or identified as such. Children as well as adults may have the disease without having recognizable symptoms. If some of these subjects carry the virus in the intestinal tract for several weeks, which according to the findings of Trask, Vignec and Paul[2] is possible, the virus must be present in relatively large concentrations in sewage during severe epidemics.

Epidemiologists in their studies of this disease have considered and investigated the possibility of indirect transmission by drinking water, food, rats, insects, birds, domestic animals and air-borne dust particles. While general sanitary conditions in areas affected by the disease have been noted, it would seem that insufficient study has been given to the possibility of infection through bathing in sewage-polluted water.

It is my conviction that there is sufficient presumptive evidence to warrant further investigation and research. The argument may be stated briefly as follows:

Since epidemic infantile paralysis occurs almost invariably during the summer, it is reasonable to assume that the disease may be spread not only by direct or indirect personal contact, but also by some agency which is effective during the warm summer months.

From the evidence in Massachusetts, the incidence of the disease during epidemics is generally highest in communities situated along the seacoast or along rivers the waters of which are subject to sewage pollution.

It has been possible to produce the disease in monkeys from the virus obtained from human stools of a case of abortive poliomyelitis as long as twenty-five days after the onset of the disease. It has also been shown that the virus in refrigerated human stools remains viable for at least ten weeks.

For every recognized case there are apparently many unrecognized cases by which infection may be spread, such cases never having shown any clinical evidence of the disease.

During epidemics, and probably at other times, the virus from active cases or from carriers is undoubtedly present in the sewage of an affected community.

Infection by way of the olfactory nerves is possible, and it appears probable that this is a common way of contracting the disease.

Given a sufficient concentration of the virus in sewage-polluted water, it is conceivable that infection can be caused by the admission of such water into the nasal passages of a bather.

While the possibility of infection by bathing in sewage-polluted water has been considered in the past and tentatively dismissed for lack of evidence, sufficient additional knowledge has been accumulated in recent years concerning infantile paralysis to warrant reconsideration of the conclusions reached by previous investigators. It is probably impossible to obtain much help from a study of the records of past epidemics. Epidemiological studies in the past have generally made no special attempt to connect the spread of infantile paralysis to bathing in sewage-polluted water. In any future epidemic it would seem advisable that more attention be given to this possibility than has been given in the past. In the meantime some further enlightenment might well be obtained through laboratory research directed toward this specific objective.

It is realized that this theory of transmission of infection has obvious weaknesses. Even though infection can be traced to a bathing-place, is it not possible that contact infection at such places is as instrumental in spreading the disease as is infection by the virus contained in polluted sewage? Can it be that the virus is present in sewage-polluted waters in sufficient concentration, even during an epidemic, to cause infection by simply being flushed through the nasal passages? These and similar questions cannot yet be answered. Here is a disease with a seasonal prevalence corresponding to the usual bathing season. In its seasonal prevalence it is more like a disease of intestinal origin than one spread by contact through droplet infection, such as measles, mumps, whooping cough and similar diseases which commonly occur during cold weather. Numerous attempts have been made to connect the incidence of the disease with some agent or condition which is effective during the summer season. Until the reason for this seasonal occurrence has been discovered, any rational theory of transmission that has not been definitely disproved deserves consideration and study. It is hoped that this brief discussion may suggest appropriate research both in the laboratory and in the field when the next epidemic occurs.

Recent investigations during the summer of 1939 have been reported by Paul, Trask and Culotta. At the International Congress of Microbiology, Paul[4] described studies made by him and his associates at Charleston, South Carolina, and Detroit, Michigan, on the successful recovery of the virus of poliomyelitis from sewage. A brief report of the work at Charleston has been published by these authors,[5] who conclude: "It is not evident from this work whether the presence of poliomyelitis virus in sewage is a direct or even an indirect link in the chain which leads this infectious agent from one patient to another in this disease. Our report merely calls attention to the fact that poliomyelitis virus may not only be present in urban sewage but also that it may be present in appreciable quantities."

Another recent discovery which may have a bearing on the theory of spread of infection by bathing is reported by Howe and Bodian.[6] They describe the infection of monkeys following the dropping of the virus of poliomyelitis into the conjunctival sac.

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ALLERGY TO TUBERCLE BACILLI AS A POSSIBLE CAUSE OF ACUTE PULMONIC CONSOLIDATION

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TUBERCULOUS lobar pneumonia is ordinarily thought of as a form of the disease in which the onset is sudden, with consolidation over an area similar in extent to that seen in pneumococcal lobar pneumonia. In the tuberculous form, instead of the consolidated area's resolving as in the pneumococcal disease, the consolidation usually goes on to caseation; the caseous tissue breaks down to form cavities and the course of the disease is rapidly and progressively downhill, death occurring within about six weeks.[1]

The case reported herewith is unusual in that while it simulated ordinary lobar pneumonia in most of its clinical features, the presence of tubercle bacilli in the sputum caused a diagnosis of tuberculous lobar pneumonia to be made, yet caseation did not occur and the patient recovered.

CASE REPORT

S. U. (No. U42829), a 28-year-old, white, married woman, entered the Massachusetts General Hospital on April 27, 1937, complaining of a "cold" which had been present for 1 week. In the past she had had frequent "colds" and for the preceding two winters they had been almost continuous, but they usually consisted only of fullness in the head, with slight nonproductive cough and occasional soreness of the throat. For 3 months before the onset of the present illness the patient had been well. One week before coming to the hospital she had noticed an aching pain in the chest, localized rather vaguely about the upper part of the sternum. Associated with this were a raw sore throat, hoarseness, malaise and chilly sensations. Two days later she began to have a hacking, nonproductive cough; the sore throat subsided but the ache extended to most of the muscles and joints, being most marked diffusely over the chest and about the neck and shoulders. On the night before entry, after going to bed she had a drenching sweat lasting 1 hour and followed by a severe chill lasting 2 hours. There had been no previous occurrence of sweats or chills, no hemoptysis, no weight loss and no known exposure to tuberculosis. The past history was otherwise irrelevant, and the family history was negative.

Physical examination showed a pale, listless young woman. The throat was slightly red; the tonsils had been removed; no enlarged lymph nodes were present. Dullness on percussion was present at the right apex and in the right infraclavicular region, and was associated with an increase in the intensity of the breath sounds, fine rales and egophony; the signs were interpreted as indicating consolidation in the right upper lobe. The physical examination was otherwise negative.

A roentgenogram of the chest on admission showed a homogeneous area of opacity involving the greater part of the right upper lobe; the lungs were clear elsewhere except for a few calcified nodes at the left hilum. The appearance was that of consolidation consistent with lobar pneumonia.

An attempt was made to type the sputum. This, however, was rather unsatisfactory because practically no sputum could be obtained. The Neufeld method gave negative results for Types 1, 2 and 4. The white-cell count was 5700 with 70 per cent polymorphonuclears, 12 per cent large lymphocytes, 8 per cent small lymphocytes and 10 per cent mononuclears. The urine was essentially normal. During the 1st hospital day the temperature rose from 101 to 104°F., the pulse from 90 to 110, and the respirations from 20 to 24. On the 2nd day the temperature, pulse and respirations remained unchanged, and the white-cell count was 7500. Sputum however was more plentiful, about 30 cc. being raised, and numerous acid-fast bacilli characteristic of tubercle bacilli were seen in the stained smear. This fact was confirmed by several observers with different preparations of the sputum. On the 4th day, while the temperature, pulse and respirations were unchanged, there was only a trace of sputum and the bacilli were less frequent; only one bacillus was present per five fields. Subsequent progress was satisfactory. The temperature returned to normal by lysis on the 6th and 7th days, with a corresponding drop in the pulse and respirations. No further sputum could be obtained for study, further white-cell counts did not exceed 6000, and the patient's general condition rapidly improved. A few hours before discharge on the 9th hospital day a roentgenogram showed almost complete resolution of the area of consolidation; there remained only a small area of decreased radiance along the right upper border of the mediastinum.

The patient spent the next 2 months at a tuberculosis sanatorium, where her condition was at all times perfectly satisfactory. All roentgenographic examinations made there were negative. A third film of the chest taken at the Massachusetts General Hospital on July 21, 1937, showed no trace of the area of consolidation. At this time the patient had gained 5 pounds in weight and was in excellent health. An x-ray film of the chest taken June 27, 1938, showed the appearance unchanged.

The association of positive sputums with a pulmonary consolidation which rapidly cleared raises the interesting questions: What was the nature of the consolidation, and what was the mechanism of its production?

The low leukocyte count, the failure to identify a causative pneumococcus and the return of the temperature to normal by lysis rather than by crisis show that this was not a case of typical lobar pneumonia. Without the discovery of the tubercle bacilli it might have been regarded as an atypical pneumonia. However, the presence of

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tubercle bacilli is not a matter to be lightly dismissed. It has been suggested that the best explanation of this and the other features of the case is that it was one of tuberculous lobar pneumonia, allergic in nature and non-caseating in its course.

The clinicopathological picture of acute caseous tuberculous pneumonia has been well summed up by Sante.[2] He points out that the consolidation, instead of clearing up rapidly as in the pneumococcal disease, persists and goes on to caseation and, as a rule, death. He mentions the possibility that the process is allergic in nature. In cases which Fränkel and Troye[3] studied they observed the subsequent occurrence of caseation in the area of consolidation and, if the patient lived long enough, cavity formation. It is not generally realized, however, that tuberculous pneumonia may instead be non-caseating. The reason that this is not well known, of course, is the much greater frequency with which caseation instead of resolution occurs as the outcome. In fact, one's first thought would be that a tuberculous process of the size present in this case would not clear in a little over a week. Nevertheless, as Wessler and Jaches[4] have pointed out, the clinical course of tuberculous pneumonia offers many surprises. They state that while the disease is as a rule ultimately, if not immediately, fatal, extensive areas of consolidation may at times resorb rapidly without the development of caseation, and that even in cases in which caseation and cavitation have occurred, recovery may sometimes take place with disappearance of the infiltration and cavities. The virulence of the toxin they consider to be the factor determining the course of events. Their discussion[5] of the subject is so complete and excellent that it should be read.

Wessler and Jaches attributed the onset of tuberculous pneumonia to overflow from an apical cavity. Such an explanation, however, would hardly be applicable to the case herewith reported. How can we explain the production of tuberculous pneumonia in a patient who presumably has been free from parenchymal involvement up to the time of onset of the pneumonia? Floyd[6] states that in thoracic tuberculous adenitis when, from caseation and softening, rupture of a lymph node into a bronchus occurs, the material may be expectorated with relief of symptoms or an inhalation tuberculous pneumonia may develop. Lord[1] likewise attributes the confluent acute or lobar form of tuberculous pneumonia to aspiration of disintegrated tuberculous material from a cavity at the apex or from a caseous node, probably to be ascribed to the effects of the toxins of the tubercle bacillus on allergic soil. Fränkel and Troye[3] were unable as a rule to recover tubercle bacilli from the sputum of patients with tuberculous pneumonia, and considered that the process in its early stages might be regarded as similar to a local tuberculin reaction. Actual allergic reactions of a similar nature have been demonstrated by Fried[7, 8] in his experimental work with the pneumococcus; he expressed the view that the acute exudate occurring in the lung following the intratracheal injection of heterologous serum depended on a state of local pulmonary allergy. He affirmed the observations of Wadsworth[9] that in animals partially or incompletely immunized against the pneumococcus a subsequent infection with highly virulent pneumococci injected intratracheally produced a lesion akin to human lobar pneumonia.

On this basis and in view of the sequence of events which occurred in the case herewith reported, it is proposed that the case was one of allergic non-caseating tuberculous lobar pneumonia. It seems reasonable to assume that this patient had been harboring an active tuberculous focus, possibly in the form of one or more infected lymph nodes, and that a state of partial immunization had been produced. One of these nodes may have gone on to caseation with aspiration of some of the infected material into the lung, and so produced an allergic response in the form of the consolidation in the right upper lobe. Of unusual interest is the fact that the process in the lung did not go on to caseation and cavity formation, but instead rapidly resolved, leaving a normal lung, and thus simulated an ordinary lobar pneumonia. The rapid recovery may have been due to this patient's having developed a higher degree of immunity than that which had been present in the cases of Fränkel and Troye; in support of this hypothesis is the evidence of the presence of calcified nodes at the left hilum.

Summary

A case is presented in which, although tubercle bacilli were present in the sputum, the clinical course and physical and roentgenological findings were those of an atypical lobar pneumonia of the right upper lobe. It is suggested that in this case a tuberculous lobar pneumonia was produced by the introduction of disintegrated tuberculous material into the lung of an individual who was in a state of partial immunity, and that the resultant consolidation was an allergic response comparable to a local tuberculin reaction. Such a process usually goes on to caseation, cavitation and death; in the case presented there was presumably a high degree of immunity so that rapid

and complete recovery occurred without demonstrable residuum.

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REPORT ON MEDICAL PROGRESS

MEDICAL ASPECTS OF OBSTETRICS

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YEARLY progress in the medical aspects of obstetrics is marked by the accumulation of evidence supporting or refuting ideas, claims and theories previously advanced by workers in the field. The discoveries arising from physiological, chemical and biological investigations must be subjected to clinical tests before their general application to clinical problems can be evaluated; hence the work of Taylor and the Smiths must follow that of Zondek and Aschheim, and the work of Colebrook and Long that of Domagk.

The report of progress made last year failed to mention the association of syphilis and the pregnant state, an omission for which I wish to make amends at the present time. It has long been known that a history of syphilis may be difficult if not impossible to obtain, and that the diagnosis of a pre-existing or even of a coincident infection in the pregnant woman may escape the usual clinical examination. It is also a matter of record, from many sources, that prompt and efficient antisyphilitic treatment, especially if applied during the first half of pregnancy, will not only reduce the fetal wastage from miscarriage and intrauterine death practically to the vanishing point, but will also similarly reduce the incidence of congenital syphilis in the newborn infant. The recent reports of Halloran,[1] Hillis and Benensohn[2] and McCord[3] are well worthy of study, as showing that the pregnant syphilitic woman who is promptly treated has at least a 93 per cent chance of bearing a healthy infant.

Since these facts are clear, the attention of the profession and of the public has been intensively directed to the advisability of routine serological examination of every gravida at the time of her first visit to the physician. Seventeen states,[4] Massachusetts included as of November 1, 1939, have more or less recently enacted laws requiring routine prenatal blood tests. It is confidently expected that this measure will reduce the incidence of congenital syphilis to a level far below that of the 78 cases reported in this state in 1937 and 1938.[4]

The problems presented by the association of pulmonary tuberculosis and pregnancy differ in considerable degree from those where syphilis is involved. In both conditions, however, early diagnosis of the pathologic state is of the greatest importance. Eisele and Mason[5] report the discovery of unsuspected pulmonary tuberculosis by stereoscopic roentgenography in 1.06 per cent of 4040 patients attending the prenatal clinic of the Chicago Lying-In Hospital and routinely fluoroscoped. Since the incidence of unsuspected tuberculosis thus discovered was approximately the same as the incidence (0.87 per cent) of unsuspected syphilis discovered by routine Wassermann and Kahn tests carried out in the same clinic over the same period of time, these writers state that routine roentgenological examinations of the chest should rank with routine serological tests as a medical necessity in pregnant women. Jameson,[6] however, in commenting upon a proposition that the New York State Department of Health study by x-ray every woman attending antepartum clinics, deprecates the idea on the grounds of the expense involved, even as a research problem, pointing out that the results of a study so conducted would fail to answer the question of the incidence of tuberculosis in pregnancy except as applied to the rather special low-income group of patients who would be seen at the state-conducted clinics.

Jameson[7] reports an investigation of the effects of pulmonary tuberculosis and pregnancy upon each other as observed at the Trudeau Sanatorium. He compares 363 tuberculous women patients be-

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tween the ages of twenty-five and thirty-five inclusive, who had had no viable pregnancies within six months preceding the development of the disease, with 54 patients of the same age group whose onset of tuberculosis either dated from a pregnancy, developed during a pregnancy or developed within six months of the termination of a full-term or viable gestation, and with 34 others who became pregnant while tuberculous. His conclusions indicate that about 12 per cent of the cases showed a possible relation between the onset of the disease and a preceding viable gestation, that symptoms appeared during pregnancy in 3.5 per cent of the cases and that 4.8 per cent dated from parturition. He found no significant difference in the death rate from tuberculosis in the patients in whom the onset of the disease was related to a full-term or viable pregnancy, as compared with a group of nulliparas of the same age group who showed lesions of similar extent.

Both Jameson, and Seeley, Siddall and Balzer,[3] the latter in a survey of 109 tuberculous gravidas, stress the importance of adequate prenatal treatment of the tuberculosis. Seeley and his co-workers pay especial attention to collapse therapy in their article, stating that the results in their series were especially good when there had been treatment for the tuberculosis before pregnancy started, and also when pneumothorax had been instituted during the first trimester.

These findings indicate the trend of results among tuberculous women whose pregnancies are not artificially terminated because of the tuberculosis per se, and re-emphasize the conclusions of Floyd quoted in last year's review.

Pneumonia occurring in pregnancy retains a place of honor among the most dreaded complications. Finland and Dublin[9] have analyzed a series of 212 cases of typed pneumococcal pneumonia complicating pregnancy and the puerperium, stating that the incidence of pneumococcal types in these cases was similar to that found in all cases of pneumonia in adults. The death rate for each decade was found to be higher for pneumonia complicating pregnancy and the puerperium than for pneumonia irrespective of the pregnant or puerperal state. The death rates were highest for late pregnancy and for women whose pregnancy was terminated during the disease. The mortality, however, in serum-treated patients was only 20 per cent, as compared with 35 per cent in corresponding non-serum-treated patients, and the authors, in analyzing the conditions contributing to the failure of serum therapy, predict that early and adequate treatment with the homologous type-specific anti-pneumococcus serums can be expected to reduce materially the high death rate from the pneumonias complicating pregnancy.

The foregoing makes encouraging reading, and it is to be hoped that sulfapyridine therapy will be of avail to lessen the mortality rate in pneumonias for which specific antiserums are still undiscovered.

The use of sulfanilamide in puerperal and postabortal infections is reported by various authors. Gordon and Rosenthal[10] state that the drug was used in large doses in 118 patients with severe puerperal infections regardless of etiology, with 38 per cent of the results prompt and satisfactory, 38 per cent unconvincing but encouraging, 20 per cent not beneficial and 4 per cent fatal. Morris[11] discusses a series of 204 puerperal and postabortal cases of infection, all cultured on admission, of which 97 were treated with sulfanilamide regardless of the organism involved. He found, as one would expect, that cases of infection limited to the uterus, vagina or perineum showed no mortality; that cases involving the pelvic cellular connective tissue, tubes, pelvic peritoneum or veins showed no puerperal mortality but a 12.5 per cent postabortal mortality in the control or untreated group; that 1 of the 2 patients with general peritonitis treated with sulfanilamide died, whereas all 3 patients in the control group died; that 3 patients with postpartum septicemia died whether or not sulfanilamide was used; and that postabortal septicemia showed a mortality of 60 per cent among 5 untreated women, while neither of 2 such patients treated with the drug died.

Much more enlightening are the articles by Chandler and Janeway[12] and by Sadusk and Manahan.[13] The former give a complete summary of the use of sulfanilamide in puerperal infections, especially those caused by the hemolytic streptococcus. They discuss the classification of these organisms, the mechanism of invasion and the role played by them in puerperal infections. They call attention to the fact that the Group A strains, which with rare exceptions are always the culprits in human puerperal infection of streptococcal origin, are normally present neither in the vagina before or after delivery in the absence of a definite infection, nor in the feces of normal pregnant women; and that puerperal septic infection is chiefly derived from the nasopharynx of contacts. They discuss in detail the method of treatment of streptococcal infections of pregnancy and the puerperium, and outline their recommendations, both for sulfanilamide treatment in the presence of a negative blood culture and for immunotransfusions in cases where the blood culture is positive, or where the clinical response to

sulfanilamide alone is unsatisfactory. Sadusk and Manahan report 2 cases of uterine infection with *Clostridium welchii,* both postabortal, one following packing of the uterus with dry gauze to terminate an early pregnancy, the other subsequent to an unsterile vaginal examination after the onset of bleeding. Both cases had positive blood cultures, but in each case the blood stream was rapidly sterilized and the patient recovered.

It seems to me that barrels of ink have been expended and tons of paper wasted in attempts to derive "results" in the treatment of puerperal infection where the bacteriology has been either unknown or, if known, has been disregarded. The pioneer work of Colebrook and his associates,[14] Lyons,[15, 16] Keefer[17] and Long, Bliss and Finestone,[18] to name but a few, has been based on knowledge and application of clinical bacteriology and immunology, those sciences the tardy application of which to puerperal infection is bringing forth such encouraging results. Although much remains to be learned, the advances of recent years are bringing us closer than ever before to a rational and effective understanding of the prophylaxis and therapy of puerperal infection.

Epilepsy associated with pregnancy has been discussed by Baptisti,[19] who reports 37 cases of gestation complicated with idiopathic epilepsy. In 21 cases the evidence showed that pregnancy had no effect on the disease; in 5 the condition was improved during pregnancy; in 4 it was made worse; and in 4 it began with pregnancy; 3 cases were unclassifiable. Clinical characteristics of the convulsion per se do not serve to differentiate epilepsy and eclampsia, as the blood pressure may be elevated during an epileptic attack and the convulsion may be followed by albuminuria. The most valuable point is the history of previous seizures, but, as this study indicates, over 10 per cent of epileptic patients have their first convulsion during pregnancy.

The question of therapeutic abortion may be raised in the case of the pregnant epileptic. To do so in the interest of the mother would appear, from Baptisti's figures, to be unjustifiable in 70 per cent of cases. On the other hand, Haupt[20] and Hoffmann[21] call attention to the danger of the occasional development of status epilepticus with its bad prognosis for the patient; and it may be necessary in the case where convulsions are much more frequent during pregnancy to consider abortion. To advise therapeutic interruption for the reason that the infant may inherit the disease is even more debatable: Baptisti quotes Lennox as reporting a heredity incidence of about 10 per cent. The recent work of Lennox, Gibbs and Gibbs,[22] reporting the occurrence, by electroencephalographic tracings, of dysrhythmia in at least one parent of 94 per cent of patients with epilepsy, suggests a greater familial predisposition than had previously been suspected. It may be that such determinations will lead in the future to a better rationale for interrupting pregnancy in epileptic patients.

No report of progress in obstetrics would be complete without some reference to the problem of hypertension and albuminuria in pregnancy, commonly known as pre-eclamptic toxemia. Numerous articles appear each year in the literature dealing with the etiology, physiology, pathology, clinical course, classification, sequelae and treatment of this complex syndrome, a few of which will be discussed.

In the matter of etiology the superficial similarity of the toxemias of late pregnancy to essential hypertension on the one hand and to nephritis on the other are matters of common knowledge. Dieckmann, of Chicago, and Reid and Teel, of Boston, have made some progress in differentiating the primary hypertension group and the secondary nephritic or vascular renal group from the welter of so-called toxemics. Dieckmann and Brown[23] maintain that the term "toxemia of pregnancy" should be restricted to those abnormal conditions in pregnancy which are characterized by the occurrence of one or more of the following signs: hypertension, edema, albuminuria, convulsions. The group includes: eclampsia, 4.4 per cent; pre-eclampsia, 47 per cent; vascular renal disease, 36 per cent; essential hypertension, 12 per cent; and acute glomerulonephritis, 0.5 per cent. Eclampsia and pre-eclampsia are distinct disease entities occurring only in pregnant women.

If these claims are substantiated, the immediate etiology of the toxemias will be found to lie primarily in essential hypertension in about half of all cases, and the ultimate causation in the factors which initiate the hypertensive state. Since Dieckmann believes that hypertension ultimately becomes vascular renal disease, the vast majority of nephritic syndromes, save only those based on glomerulonephritis and pyelonephritis, would appear to have had their inception in arterial disease.

This conclusion still leaves half the field to the conception of a pre-eclamptic–eclamptic syndrome, a theory which the obstetrician is loath to forsake. Peters[24] claims that little has been found to support the general impression that toxemias are manifestations of some abnormality of metabolism

or of disco-ordination of endocrine function. Colvin and Bartholomew,[25] on the other hand, claim that a low metabolic rate in early gestation predisposes to the eventual development of toxemia, stating that the blood cholesterol is increased above its normal level in such cases, causing vascular changes in the arteries both of the systemic circulation and of the placenta, and that at the onset of clinical toxemia the basal metabolic rate rises and the blood cholesterol level drops sharply. The development of toxemia they attribute to the trauma of fetal movements, causing rupture of placental vessels at the site of trauma and a resultant infarction, followed by the liberation of guanidine from the infarcted tissues. From the endocrine standpoint, Smith and Smith[26] find excessive amounts of prolan in the blood in 88 per cent of their toxemic and eclamptic patients, but no corresponding rise of this hormone in cases diagnosed as hypertension or nephritis. Rakoff[27] substantiates this finding in toxemic patients, but states that the findings were the same in 3 cases of nephritic toxemia. These authors are guarded in the matter of claiming any etiologic cause for toxemia in their observations, while Taylor and Scadron,[28] from similar surveys, conclude that the hormonal changes in toxemia may be simply the result of a disturbance of renal, hepatic or placental physiology.

Strauss[29] is another observer who is skeptical of the existence of "toxemia of pregnancy," claiming that 85 per cent of patients so classified have primary vascular or renal disease. The remaining 15 per cent are due, he believes, to water retention resulting from low plasma proteins, excessive sodium intake or both. While there is no doubt that some cases of toxemia may be explained on this basis, Dieckmann and Brown[23] deny that hypoproteinemia is a factor in causing toxemia.

Reid and Teel[30, 31] have made two valuable contributions to the clinical course and follow-up of the various groups of toxemic patients. Among 122 patients with known hypertension prior to and in the first trimester of pregnancy, 105 were carried through to "viability"; 70 per cent developed albuminuria, but none showed signs of renal insufficiency; 63 per cent suffered from an increase in hypertension during the last trimester. The fetal mortality in the 105 cases was 9.5 per cent. Five maternal deaths occurred in this group, 1 of postpartum amebic dysentery, 1 of eclampsia, the patient refusing adequate supervision, and 3, later, of hypertension. The subsequent history of the mothers showed continuance and eventual increase in the hypertension in practically all cases, but a surprisingly small incidence of postpartum albuminuria.

The same authors report a group of 15 patients with known glomerulonephritis occurring one to sixteen years before pregnancy. All showed albuminuria of some degree, with varying numbers of red cells and casts in the sediment from the beginning of pregnancy. Blood pressures ranged from normal to 160 systolic, 110 diastolic. No therapeutic abortions were done. During pregnancy, blood pressure and albuminuria tended to increase moderately, but only 1 case showed sudden weight gain, development of edema and shifts in body water such as occur in simple pre-eclampsia. Fourteen patients delivered live viable babies. Subsequent histories have shown that 4 of the patients are substantially worse than before pregnancy.

Reporting 235 cases of Grade 1 (mild) pre-eclampsia in which the patients were known to have normal blood pressures and urines in early pregnancy, Reid and Teel found no maternal deaths. The fetal mortality was 4.8 per cent, all viable stillbirths. Subsequent histories of the patients showed no impairment of renal function, bur 21 per cent had blood pressures of over 150 mm., three times the incidence of hypertension for women of similar age distribution irrespective of pregnancy. Fifty cases classed as Grade 2 (severe) pre-eclampsia yielded no maternal deaths, but had a fetal mortality of 26 per cent. Forty-seven of these cases were followed for six months to two and a half years after delivery, only 1 showing definite hypertension and albuminuria.

In an analysis of 168 patients treated for eclampsia at the Boston Lying-in Hospital from 1915 through 1934, Teel and Reid were able to determine that the maternal mortality was six times as high in women with eclampsia who were known to have had pre-existing hypertension or nephritis as in those known to have been normal before and during early pregnancy. Among 127 patients who had survived eclampsia there were 8 subsequent deaths: 3 had recurrent toxemia (including 2 with recurrent eclampsia), while 3 of the remaining 5 patients had hypertensive disease and 1 may have had nephritis. Eighty patients were subjected to follow-up studies: 27 per cent had some degree of hypertension, and 9 per cent albuminuria.

The studies outlined in the four preceding paragraphs, as well as those reported by Dieckmann and Brown[32] and others, bring to our attention the fact that some progress is being made toward classifying the types of hypertensive and albuminuric conditions associated with pregnancy. They indicate that pregnancy may be superimposed upon a pre-existing hypertension; that it may develop a latent hypertension which outlasts the duration of gestation indefinitely; that it may be carried success-

fully to viability in the presence of a pre-existing glomerulonephritis; that pregnancy, especially in the case of excessive multiparity and advancing age, may add appreciably to the damage done to the vascular and renal systems, as well as to the odds against the delivery of a living baby at or near term; and finally that pregnancy, whether or not it is superimposed upon a hypertensive or nephritic background, may be complicated by a syndrome of mysterious origin which for the want of a more specific etiology we must continue to call pre-eclampsia, if unassociated with convulsions, coma or both, or eclampsia, if such association occurs. Stander and Kuder's[33] concept of the low-reserve kidney may be construed as mild pre-eclampsia, though the validity of the assumption of renal primacy in this syndrome is in any event debatable. What the nature of the factor is which causes pre-eclampsia or eclampsia to occur in late pregnancy is still beyond our ken, but both the clinical behavior of these conditions and the morbid vascular physiology associated with them render the hypothesis of a circulating factor which acts as a vascular toxin, as emphasized by Page and Ogden,[34] hard to eliminate completely from consideration.

At all events, an encouraging start has been made. By the combined and co-ordinated efforts of the internist and the obstetrician and of medical and maternity clinics, or by the constant observation and study of obstetric patients before, during and for years after their childbearing careers by the physicians who attend them, we have strong encouragement for the belief that a more rational management of hypertensive and albuminuric pregnancies may be attained, and that prognosis for the life and future health of the mother and infant may be more clearly defined.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 26021

PRESENTATION OF CASE

A fifty-six-year-old housewife was admitted to the hospital complaining of pain in the chest of twenty-four hours' duration.

The patient stated that she had not been "really well" for ten years before admission. She had experienced vague, transient abdominal and joint pains, had felt weak and had noted nocturia one to three times. She, however, was able to perform her housework until eight months before admission when she developed a severe cold that left her debilitated, anorexic and listless. She began to notice nervousness, dizziness, throbbing headaches and blurring of vision. These complaints increased in severity until four months before admission when she entered the Out Patient Department. The physical examination revealed a well-developed and nourished woman in no acute distress. The fundi showed narrow, tortuous, silvery arteries, with marked changes in caliber. There were small areas of white exudate in the macular regions of both eyes. She was edentulous. The heart was enlarged to the left and downward, with the apex 11.5 cm. from the mid-sternum. A soft systolic murmur was heard over the apex, with the aortic second sound louder than the pulmonic. The rhythm was regular, the sounds of good quality, and the blood pressure 254 systolic, 134 diastolic. The lungs, abdomen and remainder of the examination were negative. The blood examination showed a red-cell count of 4,900,000 with 80 per cent hemoglobin, and a white-cell count of 12,000 with 74 per cent polymorphonuclears. The urine showed a specific gravity of 1.020, a +++ albumin test, and an abundant growth of *Bacillus coli* in the catheterized specimen; there were occasional granular and hyaline casts. A flat abdominal film showed a small right kidney and a large left kidney shadow. There were degenerative changes of the lumbar spine and evidence of arteriosclerosis. A soft-tissue mass in the true pelvis was thought to be an enlarged uterus. There was fairly prompt excretion of dye on the right side; the kidney pelves were normal in size and shape, and the ureters were incompletely demonstrated. The patient was treated symptomatically, but her complaints progressed. One month before admission to the hospital daily vomiting began, and persisted. Her vision failed, and she became dyspneic, and orthopneic, but noticed no edema. She felt very drowsy but, at the same time, restless and was unable to sleep. One week before entry she noted that her urinary output had become scanty. One day before admission the abrupt onset of a severe substernal and mid-epigastric pain appeared; there was no radiation to the neck, jaw or arm. The pain was so agonizing that it caused her to "double up," and she felt choked and as though she could not breathe. The pain kept her awake all night, but diminished somewhat on the morning of admission. There was an associated severe headache. She had lost 30 pounds during the eight months before admission. The remaining past, family and marital histories were noncontributory.

The physical examination revealed a sallow, well-developed woman with loose skin and evidence of recent weight loss. She was listless and responded poorly. The breath was uriniferous. The fundi showed areas of exudate, silver-wire arteries with marked changes in caliber, and blurred optic disks with loss of physiologic cupping. The heart was enlarged to the left and downward, with a systolic murmur over the precordium. There was also a harsh scratching sound heard in systole over the pulmonic area and along the left border of the sternum. The blood pressure was 240 systolic, 140 diastolic. The radial and brachial arteries were extremely hard. By vaginal examination the fundus of the uterus seemed to be about twice its normal size, but was firm and freely movable; the cervix was normal.

The temperature was 99°F., the pulse 90, and the respirations 22.

Examination of the blood showed a red-cell count of 3,100,000 with 69 per cent hemoglobin, and a white-cell count of 15,300 with 94 per cent polymorphonuclears. The urine showed a constant ++++ albumin test, with the sediment containing innumerable white cells. A urine concentration test demonstrated a maximum specific gravity of 1.014. A culture of a catheterized specimen showed no growth. The serum nonprotein nitrogen was 130 mg. per 100 cc. The serum calcium was 7.7 mg. per 100 cc., and the phosphorus 14.0 mg. A lumbar puncture was normal except for a ++ ammonium sulfate ring test and a total protein of 63 mg. per 100 cc. An electrocardiogram taken one day after admission showed a low T_1, a diphasic T_2 and an inverted T_3, with Q_3 small, ST_1 and ST_2 slightly depressed, and slight slurring of QRS. A retrograde pyelogram

on the left showed the tip of the catheter at the level of the upper margin of the sacrum; the kidney pelvis was moderately dilated, the calyces were irregularly outlined, and the ureter was not dilated. The patient ran a slow, steadily downhill course. A few hours after admission she became more restless, and dyspneic. She became cold and gray, and was sweating. The pericardial friction rub disappeared, and the pulmonic second sound became louder than the aortic. The right lung filled with fine crackling inspiratory rales, and a gallop rhythm appeared at the apex. The blood pressure remained at 280 systolic, 140 diastolic. She became irrational, stuporous and finally, after a few days, comatose. Her serum nonprotein nitrogen rose to 205 mg. per cent. The temperature gradually rose to 100, then to 103°F., where it remained for three days until she died on the tenth hospital day. The pulse varied between 80 and 100, and the respirations from 12 to 25. A few hours before death she developed a confluent erythematous eruption over the entire body.

Differential Diagnosis

Dr. William B. Breed: This on the surface seems to be a perfectly orthodox case. It is that of a fifty-six-year-old woman with ten years of disability and increasing symptoms which suggest arteriosclerosis, hypertension and nephritis. Through the period of the visits to the Out Patient Department there seems to be very little to comment on except the question of the condition of the left kidney, which is not clearly described. In the Out Patient Department the urine at first showed an abundant growth of colon bacilli but no pus; later on, much pus and a sterile culture. She had no substernal or epigastric pain until just before she came into the hospital, so that we do not have to consider anything else but progressive arteriosclerosis with hypertension and nephritis, except possibly the question as to what part one kidney played in the production of hypertension. The report on the intravenous pyelogram is not at all conclusive, and I should like a little more information on that.

Dr. George W. Holmes: We have here only the films of the retrograde pyelogram; those of the previous intravenous pyelogram are missing. The report of the latter speaks of a large left kidney and a small right one; it mentions fairly prompt excretion of the dye by the right kidney and implies but does not actually state that excretion was delayed on the left. They did not describe any abnormality of either pelvis but nevertheless interpreted the findings as suggestive of left hydronephrosis. I should not care to accept such an opinion without reviewing the films myself.

These are the films of the retrograde pyelogram. We have no films that are free from motion, and I imagine that they were taken with low-amperage apparatus. The left kidney is a little larger than the right. The right is small, and the left about normal in size. I should not interpret this pyelogram as being abnormal. The left pelvis does look large, but if the man who injected it used a little more pressure than usual he could make a normal kidney pelvis look as large as that and assume that shape. Whatever change you have there might be due merely to spasm from overinjection. The kidneys may be diseased, but I am not willing to make a diagnosis of anything in particular from the evidence.

Dr. William B. Breed: She may have had infection in both kidneys or only in one. While in the hospital the fever was indicative of a generalized infection. Up to the day before entry this is a perfectly straightforward story of increasing renal failure and hypertension. The episode which occurred on that day could have been due to one of three important things: coronary occlusion, pericarditis or pulmonary embolus. We do not need to consider anything but pericarditis if we are going to be consistent. The pain is perfectly admissible. She did not have shock; she had no fall in blood pressure. At that time there was a systolic friction rub over the pulmonic area and along the left sternal border, but no evidence of a large pulmonary embolus or of a coronary episode.

Before this exercise, I took the occasion to talk with Dr. Bland about the electrocardiogram, without telling him the story, because I was confused about it. I think it would be fair to ask him now, knowing the story, to comment further. She had had no digitalis to produce the changes. She did have uremia, which might explain them. The only thing that was odd about it was the absence of left-axis deviation, in the face of a large left ventricle.

Dr. Edward F. Bland: This tracing is well described in the record. It is abnormal but without a very characteristic configuration. ST_1 and ST_2 are definitely low and diphasic. T_3 is a little inverted. The QRS complexes are just a little slurred but within the accepted normal. The chest lead is normal. The PR interval is at the upper limit of normal, 0.2 sec., which was not mentioned in the record. With these changes one would suspect that digitalis was responsible, but the patient is said to have had none. These

changes in the ST waves in all three leads make one wonder a little about pericarditis. Uremia also will change the T waves, as well as other severely toxic states. If this patient had a big heart secondary to hypertension, it is a little unusual not to have had a little more indication of left-axis deviation, but I do not believe we had better put too much weight on that.

DR. BREED: Would the presence of pericarditis or pulmonary infarct destroy the evidence of left-axis deviation that might have been there.

DR. BLAND: If there had been left-axis deviation due to hypertension, it would have taken a considerable amount of dilatation of the right side of the heart to balance it in a normal direction. We sometimes see such a condition in young people with severe rheumatic fever who get acute dilatation of the heart. One also has to consider that there may have been very clear changes due to coronary disease before the last episode, which may in turn have masked them.

DR. PAUL D. WHITE: I should consider this an abnormal record. Dr. Breed will remember a patient whose record improved in appearance a good deal while coronary disease actually increased, due to a compensating lesion in a different part of the heart. With an old apical infarct the T waves in Lead 1 were inverted, but a fresh, basal infarct made them upright again and so look better. Actually the patient was sicker as a result of the new lesion.

DR. JOHN H. TALBOTT: Is it clear that the patient had not had digitalis before the electrocardiogram was taken?

DR. TRACY B. MALLORY: On the day before, at three in the afternoon, the patient had been given 9 gr. Some time earlier, while being followed in the Out Patient Department, she had been given digitalis, but she had not taken any for several months.

DR. BREED: In any case, digitalis may have had an effect on the tracing. The electrocardiogram does not give us much help in determining what was going on here except, I think, in ruling out coronary occlusion.

I shall comment a minute on the blood chemical findings. At first glance the figures suggest hyperparathyroidism, but the phosphorus is a good deal higher in proportion to the depression of the calcium than one finds in that condition. I think these figures merely represent a very severe acidosis, which is always present with this degree of uremia.

If I am right, the first episode of pain, before she came in, is to be accounted for by pericarditis associated with uremia. The pulmonic second sound became much louder than the aortic, a change which suggests that in addition to uremia and pericarditis there may have been pulmonary infarction toward the end. Of course, this change in the pulmonic second sound is very striking, if the record is true, and I think it is worth taking seriously. At about the same time they found crackling inspiratory rales, and a gallop rhythm in the heart. There is no note of distended neck veins. If she had had distended neck veins it would make it a little easier to conclude that there was pulmonary infarction. I am rather inclined to think that this last episode of pain is different from the one she had before she came in, and that it was perhaps due to pulmonary infarction. We know she had infection in the genitourinary tract, which involved one or both kidneys. She had been sick a good while, and there is every reason to expect that she might have had an embolus, septic or not.

So to summarize, she had arteriosclerosis and uremia, the latter probably on an arteriosclerotic-hypertensive basis. Not being able to accuse one particular kidney I cannot include it as a cause of the hypertension, although there might perfectly well have been a contributory infection in the kidney. As a terminal event, pericarditis supervened. I suspect that in addition there may have been terminal pulmonary infarction.

DR. WHITE: I should like to comment on the scratchy sound in systole over the pulmonic area that disappeared. We have observed it a number of times in cases without pericarditis but with acute pulmonary embolism and resulting dilatation of the pulmonary artery. I think it might be explained on that basis in this case; in other words, the first attack might have been due to pulmonary embolism rather than pericarditis and another attack occurred later.

DR. BREED: Apparently the friction rub lasted ten days or more. She was in the hospital for ten days, and it only disappeared the day before she died. One would not expect a pulmonary affair to remain constant for ten days.

DR. WHITE: True, but there may be prolonged dilatation of the pulmonary artery, as in cases of thyrotoxicosis. I have not known of its persistence for as long as ten days in pulmonary embolism, however.

DR. TALBOTT: I saw the patient only a couple of days before she died. The pericardial friction rub had disappeared.

DR. WHITE: So it may have been brief.

DR. BREED: It could have been due to pericarditis and still have disappeared.

DR. WHITE: I was trying to help you out with

one diagnosis so you would not have to make two.

DR. BREED: Then you would like to exclude pericarditis, if possible?

DR. WHITE: Yes. The pericardial friction rub in uremia is near the apex and the lower end of the sternum rather than over the pulmonic valve area.

DR. BLAND: Might I ask about pain associated with pericarditis. Is it usually as agonizing and severe as it apparently was here? My impression is that most people with pericarditis have no severe pain.

DR. BREED: I should agree, but it may be very severe.

DR. WHITE: The pericarditis of uremia is painless, is it not?

DR. BREED: Not always.

DR. MALLORY: A significant number of patients with pericarditis reach the operating table and have their gall bladders or stomachs explored.

DR. CHARLES L. SHORT: That point came up before at one of these conferences. It was said that many of these patients were stuporous and did not notice the pain, but that in conscious patients it was a common finding.

DR. BREED: May I ask whether this electrocardiogram rules out a pulmonary embolism in the first episode?

DR. BLAND: There are no characteristic changes of acute pulmonary embolism in the record.

DR. WHITE: It may be too late for them. The record was taken twenty-four hours after the attack. The electrocardiographic evidence in the acute cor pulmonale may last only a few hours.

CLINICAL DIAGNOSES

Uremia.
Vascular nephritis.
Coronary occlusion?

DR. BREED'S DIAGNOSES

Arteriosclerosis.
Arteriosclerotic and hypertensive heart disease.
Acute pericarditis.
Vascular nephritis (uremia).
Pulmonary emboli?

ANATOMICAL DIAGNOSES

Vascular nephritis, chronic.
(Uremia.)
Pericarditis, fibrinous, acute.
Cardiac hypertrophy, hypertensive type.
Arteriosclerosis of coronaries, aorta and renal vessels.
Hydronephrosis, left, slight.
Leiomyomas of uterus.
Cystitis.

PATHOLOGICAL DISCUSSION

DR. MALLORY: Cases of this sort are difficult to interpret in life and equally difficult to interpret after postmortem examination. This patient did have a pericarditis, an acute fibrinous one, and did not have any pulmonary emboli. So I think we have to assume that the rub and pain were both due to pericarditis. She had a moderate amount of coronary sclerosis but no occlusion and no areas of infarction. The heart was considerably hypertrophied, weighing 600 gm., and the hypertrophy was predominantly left ventricular. So it seems she would have had a left-axis deviation.

The kidneys are rather more difficult to interpret. They were a little small—one weighed 120 gm., the other 135 gm. The pelvis of the left kidney seemed to us very slightly dilated, and the calyces very slightly blunted. On the right the pelvis was even more questionable; we were not sure whether it was dilated. The renal arteries on both sides showed rather marked atheromatosis, and on the left, one of the atheromatous plaques seemed definitely to obstruct the lumen of the artery. Both kidneys showed adherent capsules and granular surfaces, and on microscopic examination, an extremely severe grade of vascular nephritis. Whether or not they show minimal evidence of inactive and healed pyelonephritis, I would not dare to say. I can see nothing that strikes me as convincing evidence of such a diagnosis, although I think it is the type of lesion that might be interpreted as such.

DR. WHITE: Was the pericarditis fibrinous and not purulent?

DR. MALLORY: It was fibrinous.

DR. HOLMES: Was there any disease of the mucous membrane of the pelvis of the kidney?

DR. MALLORY: No.

DR. WHITE: An important lesson from this case is the correction of the current impression, which had been my own also, that the pericarditis of uremia is painless. Terminal heart failure may explain the late signs which simulated a final pulmonary embolism.

CASE 26022

PRESENTATION OF CASE

A sixty-three-year-old Italian candy maker was admitted complaining of difficulty in eating solid food.

Four years before entry the patient had retired from active business but felt quite well at that time. For the next two years his health remained good, but thereafter he gradually developed ma-

laise and progressive weakness. There was slight increasing dyspnea with exertion but no cough or expectoration. For about eight months prior to admission he had swelling of the ankles developing in the afternoon and subsiding during the night. There was no associated pain or intermittent claudication. Four months before entry he began to have nocturia of four or five times, with a diurnal frequency of five or six times. There was some dysuria, but the urinary symptoms were improved following medication two weeks before admission. Two months before entry he began to have difficulty in swallowing. There was some question in the recorder's mind as to whether this was obstruction or merely an extreme anorexia. The patient stated that he would take a mouthful of food and then expectorate it. He was able, however, to ingest liquids without difficulty. There was some gaseous eructation, but no nausea or vomiting. During the four months before coming to the hospital he was slightly constipated and took a laxative every other day. This produced two bowel movements daily, which were not watery and did not contain blood. The stools were rather light colored, but there was never any jaundice. Two months before entry he first noted that his abdomen was larger than usual. There was no pain except for occasional lower abdominal cramps associated with bowel movements. A week before entry he began to cough up small amounts of mucoid material. Occasionally a little blood was expectorated in the morning. The cough often awakened him at night, and he had difficulty in getting his breath until he raised some of the mucoid material. At no time was the patient confined to bed. His weight five years previously was 188 pounds, and on entry 176 pounds.

Physical examination showed a well-nourished, florid man who coughed frequently. There were numerous telangiectases on the face; the skin, nailbeds and mucous membranes were hyperemic. Oral hygiene was poor, and the tongue was dry and furred. Percussion of the chest showed that the diaphragm was higher than normal, with the left leaf higher than the right. There was dullness at both apices posteriorly, and inconstant rales were audible at the right apex; no other pulmonary signs were noted. The heart was slightly enlarged to the left, and the sounds were distant in character; no murmurs were heard. The abdomen was protuberant, and there was a reddish-blue, reducible, umbilical hernia. A fluid wave was elicited, and there was shifting dullness in the flanks. The liver and spleen were not palpable, but there was tenderness in the right upper quadrant. The left testicle was small, and the scrotum over its posterior surface presented a rough hard area. There were numerous varicosities of the lower extremities, and pitting edema up to the hips.

The temperature was 99.8°F., the pulse 100, and the respirations 25.

Examination of the urine showed a specific gravity of 1.032, with a slight trace of albumin and a green precipitate with the Benedict test. The blood showed a red-cell count of 4,600,000 with a hemoglobin of 90 per cent, and a white-cell count of 7590 with 81 per cent polymorphonuclears. Several sputum specimens contained blood but were negative for tubercle bacilli. Three stool specimens gave negative reactions to the guaiac test. A blood Hinton test was negative. The icteric index was 5, and the van den Bergh test gave a direct reaction. A liver function test showed 40 per cent retention of dye, and the Takata-Ara reaction was strongly positive. A tuberculin test was negative.

X-ray examination showed a diaphragm with limited motion. There were increased markings in the medial portions of both lower lung fields and a hazy, partially calcified dullness in the lateral portion of the first right intercostal space. The heart was not enlarged, but the left ventricle appeared to be hypertrophied. The aorta was tortuous and slightly widened, and showed marked calcification. There was no evidence of esophageal varices, but the lower end of the esophagus was dilated and there was a small hiatus hernia.

On the second hospital day 3500 cc. of slightly cloudy, pale-yellow fluid was removed by abdominal paracentesis; this formed a pellicle on standing. The specific gravity was 1.005; there were 300 white blood cells per cubic millimeter, of which 75 per cent were lymphocytes and 25 per cent polymorphonuclears. The patient continued to run a fever up to 100°F. and on the fourth hospital day expectorated about half a cupful of reddish-brown sputum. Six days later the temperature rose sharply to 103°F., and the respirations to 45. There was dullness at the right base. The breath sounds were diminished, and a few crackling rales were heard. Later the dullness became increased and bronchial breathing was heard in the same region. His temperature remained elevated, and the chest signs persisted. His condition became progressively worse, and he died on the thirteenth hospital day.

Differential Diagnosis

Dr. Alfred O. Ludwig: The differential diagnosis in this case presents considerable difficulty because of the fact that his symptoms are referable to several systems. The most important features in this history seem to me to be the increas-

ing dysphagia, the dyspnea, the cough and later hemoptysis, the malaise and weight loss, the abdominal symptoms, the increase in size of the abdomen, the cramps and constipation, and finally the increasing edema of the lower extremities.

The record tells us that this man had not lost much weight. The telangiectases mentioned are not unusual in older individuals, but are thought by some to be indicative of liver disease. The examination of the lungs indicates that both leaves of his diaphragm were high, and further information makes it likely that they were elevated by the presence of fluid in the abdominal cavity. I am inclined to discount the lung findings mentioned at this point. Along with everything else, the presence of an umbilical hernia is confirmatory evidence that there was an increase in intra-abdominal pressure, in this case due to fluid. I do not know how to interpret the findings in the testicle and scrotum. The edema of the lower extremities was probably due to the same cause as was the ascites.

The laboratory examination proved that this individual did not have any marked degree of renal disease, as he was able to concentrate up to a specific gravity of 1.032. This is unusually high and may be partially explained on the basis of glycosuria, although he may have been somewhat dehydrated at the time this specimen was collected, or was unable to excrete water normally because of the edema. The examination of the blood was normal, but the presence of blood in the sputum draws our attention back to the lungs, and it is difficult to escape the idea that there must have been some lesion there to explain this finding. The absence of occult blood in the stool is a bit of evidence against a lesion which would cause bleeding into the gastrointestinal tract, such as cancer of the stomach or bowel, and also against varices in the esophagus, at least against bleeding varices. The icteric index and van den Bergh tell us that there was a disturbance of the liver, and as we know that there was bile in the stools, the bilirubinemia could not have been due to an obstruction of the bile passages but must have been secondary to disease within the liver. This is further substantiated by the fact that he had a markedly impaired liver function, as evidenced by the retention of 40 per cent of the dye and also by the strongly positive Takata-Ara test. This is good evidence of severe liver damage, although it does not tell us anything about its cause.

The x-ray films of the lungs are consistent with the presence of an old tuberculosis, but I cannot tell from them whether there was active tuberculosis at the time of his entry. The findings in the heart and aorta I interpret as consistent with his age. I should like to know more about the dilatation of the lower end of the esophagus. One wonders, for instance, if there might have been some cause for obstruction below. Certainly the record should so state, if there was any evidence of esophageal tumor. A hiatus hernia is not uncommonly present, and I do not believe that it contributes to his symptoms.

The findings in the ascitic fluid are those of a transudate, but I do not believe that ordinary transudates, such as one would expect to find in uncomplicated hepatic cirrhosis, usually contain so many white blood cells, and their presence suggests a complicating low-grade peritonitis, which is not uncommon in the presence of cirrhosis of the liver.

The terminal course of this patient again leads us back to the lungs. The description is that of a pneumonic consolidation at the right base, and this condition seems to have led to his death.

Is it possible to tie up all these findings and to explain the course of the disease on the basis of one diagnosis? I do not believe that it is. In the presence of marked impairment of liver function, jaundice and edema, I do not see how one can escape the diagnosis of cirrhosis of the liver. We do not know if he had an alcoholic history, but that is not necessary for the development of cirrhosis. However, such a diagnosis cannot explain the hemoptysis, cough and dyspnea, and terminal lung findings, and we must conclude that the dullness and rales heard at the apices at the time of admission are more important than I was at first inclined to believe. These, plus the x-ray findings, as well as the persistent hemoptysis, strongly suggest the presence of pulmonary tuberculosis. If this is true, then even the terminal event could be explained on the same basis, namely, a tuberculous pneumonia, arising by a sudden massive bronchial spread. The presence of the white cells in the peritoneal fluid might be interpreted as evidence of a low-grade tuberculous peritonitis, although there is nothing else to suggest it, and implies that he had a miliary spread at the end. This is possible, but we have no way to be certain. The negative tuberculin test is against the diagnosis, but may occur occasionally in the presence of miliary tuberculosis.

Is there any other way in which we can explain his symptoms? I suppose that one should consider tumor of the lung. Metastatic carcinoma does not usually invade bronchi and therefore does not cause hemoptysis. It would seem to me to be very unlikely that this man had a large primary bronchial carcinoma without there being

more evidence of it on physical or x-ray examination.

Could he have had tumor elsewhere? If present, it must have invaded the liver to the extent that it caused marked impairment of function, and in that case it would seem likely that the liver would have been enlarged and that metastatic masses would have been palpable. It is possible of course that he may have had a primary hepatoma arising on a cirrhotic liver, a favorable condition for such an event. I do not believe that we have enough evidence for this diagnosis. Should one consider that tumor may have arisen from the testicle? If it is of any importance at all, I think it is more likely that the mass felt there was tuberculous, and part of a general tuberculosis. How about the terminal dysphagia? It may have been a part of his cirrhotic symptom complex, but I do not recall having seen such marked dysphagia from that cause alone. As no intrinsic cause was demonstrated, and there does not seem to have been a paralysis of the pharyngeal muscles, one must consider an extrinsic cause for this symptom. Possibly there were lymph nodes which were causing pressure on the esophagus. If so, they should have been demonstrated by x-ray. I do not believe that this is an entirely satisfactory explanation. In the absence of a blood-sugar determination, it is not possible to say whether the glycosuria was due to diabetes mellitus or related to the liver disease. It was more likely due to the latter. There was no evidence of renal tuberculosis.

It is possible that the liver impairment was tuberculous in origin, either due to large tuberculous foci in the liver or to miliary tuberculosis. If he had miliary tuberculosis, it must have been of very recent origin, as his whole story is much more that of slowly developing symptoms secondary to hepatic cirrhosis, with perhaps a terminal lighting up of an old tuberculous process in the lung.

Clinical Diagnoses

Cirrhosis of liver.
Bronchopneumonia.
Ascites.
Malignancy of lung?
Tuberculosis of lung?

Dr. Ludwig's Diagnoses

Portal cirrhosis of liver.
Ascites and peripheral edema.
Pulmonary tuberculosis (apical and tuberculous bronchopneumonia).
Tuberculous peritonitis?
Miliary tuberculosis?

Anatomical Diagnoses

Cirrhosis of liver, alcoholic.
Ascites.
Lobar pneumonia.
Pulmonary tuberculosis, healed.
Peritonitis, chronic aseptic.
Nephritis, chronic vascular, slight.

Pathological Discussion

Dr. Tracy B. Mallory: The clinicians on the ward who were in charge of this patient reached essentially the same conclusion as that of Dr. Ludwig. The primary condition was obviously cirrhosis of the liver. The organ was moderately hypertrophied, weighing 1950 gm. Its surface was definitely granular, with fairly uniform nodules measuring from 1 to 4 mm. in diameter. It was markedly firm and cut with considerable difficulty, thus indicating extensive fibrosis. On microscopic examination it was entirely consistent with an alcoholic cirrhosis, and the lack of a definite history may well have been due to the language difficulty and the necessity of taking his story through an interpreter. Considering the severe degree of the cirrhosis, it was surprising that the spleen was not enlarged. It weighed only 160 gm. and did not show any significant degree of the fibrotic change which is usual in cases of portal obstruction. The esophagus also showed little abnormality, although the prosector thought there was a slight dilatation of some of the mucosal veins; certainly there were no definite varices. In the clinical examination it was noted that the veins of the anterior abdominal wall were unusually prominent, and it is possible that most of the collateral circulation had developed in this direction rather than through the splenic vein and the esophageal vessels. His omentum was very densely adherent in both flanks and beneath the old herniorrhaphy wound, which may well have permitted an extensive collateral circulation to have developed. We found nothing which would explain the dysphagia. An old apical tuberculous process was present, but there was no definite evidence of activity. The terminal event was a lobar pneumonia in the right middle and lower lobes. The heart was not hypertrophied, and the coronaries showed moderate atherosclerosis but no significant narrowing of their lumens. The kidneys showed a moderate grade of vascular nephritis, and unfortunately, we did not explore the testicle. The peritoneal fluid was very faintly turbid, and the peritoneal surfaces tended to be slightly granular; nothing was found, however, to suggest a true infectious peritonitis.

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THE TUBERCULIN PATCH TEST

In 1937 Vollmer and Goldberger[1] described a tuberculin patch test for children and found it simple, harmless and reliably approximating the accuracy of the Pirquet test. The material for this Vollmer patch test consists of a wide strip of adhesive tape on which have been placed two small squares of filter paper previously saturated with Old Tuberculin, with a control square saturated with glycerin broth between them. The tape with its dried squares is firmly applied to the skin, previously cleansed with ether, benzol or acetone. Natural moisture of the skin (insensible perspiration) liquefies the tuberculin concentrate, which can then be absorbed by the skin, producing a tuberculin reaction. The tape with its squares is removed forty-eight hours later, and the test is read forty-eight hours after removal. A few tests may not become positive until the third or fourth day.

Vollmer and Goldberger[2] carried out a comparative study of the patch test and the Mantoux test in 678 children. Their results showed 100 per cent conformity of the patch test with the Mantoux test using 0.1 mg. of Old Tuberculin or the first test solution of Purified Protein Derivative. Hart[3] in England found similar results in comparative studies on 536 children, but the patch test gave fewer positive reactions than did strong dilutions (1.0 mg.) of Old Tuberculin. Wolff and Hurwitz[4] tested 964 children under sixteen years of age. They found no discrepancy between the patch test and Mantoux test in cases with active tuberculosis, but one of 1.8 per cent in the series as a whole. Another comparative study on children twelve to sixteen years of age is reported in this issue of the *Journal*.

Experience is thus accumulating to show that the tuberculin patch test is a new and important addition to our armamentarium in the early diagnosis of tuberculosis. It is a test that is simple and painless to carry out, and one that requires no instruments to perform. Severe local and constitutional reactions have not been reported, and there is no danger of infection. There is little objection to its use, and it is a test that should prove of value to the practitioner in the use of tuberculin for the discovery of contact cases of tuberculosis. The difficulties that are entailed in the preparations for a Mantoux test and the ever-present fear of the "needle" by both parents and children too often lead to its omission as a diagnostic procedure.

The conformity of the tuberculin patch test to the Mantoux test using 0.1 mg. of Old Tuberculin or the first test solution of Purified Protein Derivative has been well established in children, but comparative studies in adults are lacking. Until more widespread investigations have been carried out it is probably still necessary, as recommended by Vollmer and Goldberger,[2] to retest those negative to the patch test with 1.0 mg. of Old Tuber-

culin or the second test solution of Purified Protein Derivative. Where there is any doubt regarding the presence of tuberculous infection the Mantoux reaction remains the final and deciding test.

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INDUSTRY AND SYPHILIS

In the present campaign against syphilis attention should be called to the important relation of industry, as represented by employers, to syphilis. Syphilis produces incapacity in workers in two stages: first, in the early stage when it is communicable; and, secondly, in the late stage when manifestations of the disease produce a lowered earning capacity. If early syphilis is adequately treated the contagiousness quickly disappears and the individual can return to work with an excellent chance of continuing an undiminished earning capacity. If employers see to it that such a worker continues his treatment and keep him on the job, they can retain such people as valued workers and aid in preventing the later disabling consequences which may result in the worker's becoming a public charge because of cardiovascular or cerebrospinal complications. Surveys have shown that in patients observed over a ten- or twenty-year period no cases of syphilitic heart disease developed among those who had received proper treatment in the early stages, while 3.4 per cent of those having no treatment developed cardiac manifestations. Furthermore, in these series only 1.6 per cent of the properly treated patients showed central-nervous-system disease, while in the untreated cases 17 per cent of the patients developed syphilis of the central nervous system. All in all, it has been found that adequate treatment early in the disease will prevent the manifestations of late syphilis in more than 80 per cent of all cases.

In the majority of cases discovered at present the patients are found to have the latent and asymptomatic type of syphilis, and the late complications may also be prevented in these cases by adequate treatment. Some industries have already established clinics for the treatment of infected employees and their families and are requiring routine serological examinations. These employers are not discharging such employees. They require them to continue treatment. They preserve the relations of the worker and the medical department in the best professional tradition. Such employers are to be commended for thus contributing to the advance of preventive medicine.

This matter has been considered of sufficient importance by the United States Public Health Service* to warrant the advocation of a special program concerning the handling of syphilis among employees. The recommendations are:

> That routine blood tests be taken on applicants for employment.
>
> That routine blood tests be taken at the time of periodic re-examination of employees.
>
> That industry, with its compact organization, develop a vigorous educational program.
>
> That industry extend its educational campaign into the field of prophylaxis.
>
> That responsibility upon the industrial medical officer to see that adequate modern treatment is available to employees at prices ordinary wage earners can afford be fully recognized. If such treatment is not available in private practice or at public clinics, industrial medical service should undertake such treatment.
>
> That syphilis be handled, at all times, as merely another communicable disease. The privacy of relations between the worker and the medical service should be preserved in the best professional tradition. When treatment is properly required, in ordinary cases this cannot be regarded as ground for discrimination of any kind against employees.

If all physicians having part-time or full-time positions with industrial concerns are willing to co-operate in urging the adoption of this program by industry, much will be gained toward the eradication of syphilis and the prevention of lowered earning capacity due to its late manifestations.

*Release (No. 15-91) from United States Public Health Service, dated January 6, 1939.

MEDICAL EPONYM

Addisonian Anemia and Addison's Disease

At a meeting of the South London Medical Society on Thursday, March 15, 1849, according to an unsigned report of the proceedings published in the *London Medical Gazette* (N. S. 8: 517 – 518, 1849), it is stated:

> Dr. Addison, at the request of the President, proceeded to describe a remarkable form of anaemia, which, although incidentally noticed by various writers, had not attracted, as he thought, by any means the attention it really deserved. . . . It was . . . incident to adult males . . . usually occurs between the ages of twenty and sixty . . . more frequently commencing insidiously and proceeding very slowly . . . relaxation and flabbiness, rather than wasting of the flesh, being one of the most remarkable features of the disorder. Dr. Addison next proceeded to give the details of several cases [of another disease] which had fallen under his own immediate observation. In only two of these did the patients recover. . . . In three cases only was there an inspection of the body after death, and *in all of them was found a diseased condition of the supra-renal capsules.*

The above is the first published reference to Addison's description of these two diseases.

Thomas Addison (1793 – 1860), then senior physician to Guy's Hospital, London, published his famous monograph, ***On the Constitutional and Local Effects of Disease of the Supra-Renal Capsules*** (London: Samuel Highley), in 1855, in which appear the following accounts (pages 2 and 3, and 4 and 5):

> For a long period I had from time to time met with a very remarkable form of general anaemia, occurring without any discoverable cause whatever; cases in which there had been no previous loss of blood, no exhausting diarrhoea, no chlorosis, no purpura, no renal, splenic, miasmatic, glandular, strumous, or malignant disease. Accordingly, in speaking of this form of anaemia in clinical lecture, I, perhaps with little propriety, applied to it the term "idiopathic," to distinguish it from cases in which there existed more or less evidence of some of the usual causes or concomitants of the anaemic state.
>
> The disease presented in every instance the same general character, pursued a similar course, and, with scarcely a single exception, was followed, after a variable period, by the same fatal result. It occurs in both sexes, generally, but not exclusively, beyond the middle period of life, and so far as I at present know, chiefly in persons of a somewhat large and bulky frame, and with a strongly-marked tendency to the formation of fat. It makes its approach in so slow and insidious a manner, that the patient can hardly fix a date to his earliest feeling of that languor, which is shortly to become so extreme. The countenance gets pale, the whites of the eyes become pearly, the general frame flabby rather than wasted; the pulse perhaps large, but remarkably soft and compressible, and occasionally with a slight jerk, especially under the slightest excitement; there is an increasing indisposition to exertion, with an uncomfortable feeling of faintness or breathlessness on attempting it; the heart is readily made to palpitate; the whole surface of the body presents a blanched, smooth and waxy appearance; the lips, gums and tongue seem bloodless; the flabbiness of the solids increases; the appetite fails; extreme languor and faintness supervene, breathlessness and palpitations being produced by the most trifling exertion or emotion; some slight oedema is probably perceived about the ankles; the debility becomes extreme, the patient can no longer rise from his bed, the mind occasionally wanders, he falls into a prostrate and half-torpid state, and at length expires: nevertheless to the very last, and after a sickness of perhaps several months' duration, the bulkiness of the general frame and the amount of obesity often present a most striking contrast to the failure and exhaustion observable in every other respect.
>
> With, perhaps, a single exception, the disease, in my own experience, resisted all remedial efforts, and sooner or later terminated fatally. On examining the bodies of such patients after death, I have failed to discover any organic lesion that could properly or reasonably be assigned as an adequate cause of such serious consequences. . . .
>
> It was whilst seeking in vain to throw some additional light upon this form of anaemia, that I stumbled upon the curious facts, which it is my more immediate object now to make known to the Profession. . . .
>
> The leading and characteristic features of the morbid state to which I would direct attention are anaemia, general languor and debility, remarkable feebleness of the heart's action, irritability of the stomach, and a peculiar change of colour in the skin, occurring in connexion with a diseased condition of the "supra-renal capsules."
>
> . . . This discoloration pervades the whole surface of the body, but is commonly most strongly manifested on the face, neck, superior extremities, penis and scrotum, and in the flexures of the axillae and around the navel. It may be said to present a dingy or smoky appearance, or various tints or shades of deep amber or chestnut-brown; and in one instance the skin was so universally and so deeply darkened, that, but for the features, the patient might have been mistaken for a mulatto.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY*

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Fatal Puerperal Sepsis Following Normal Delivery

Mrs. M. C., a thirty-six-year-old woman, was admitted to the hospital on July 14, 1926, with a temperature of 102.6°F. and a pulse of 100. Her fifth baby had been delivered normally at home thirteen days previously. She stated that, after

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

having been well since the birth of the baby, she felt poorly and complained of a good deal of pain and soreness in the lower abdomen on getting out of bed on the tenth day. The baby died on that day.

The family and past histories were not recorded, except that it was noted that the first pregnancy had resulted in a miscarriage at three months and that the next four babies were all delivered normally but died in infancy.

Physical examination on entrance showed a patient who was apparently not seriously ill. The breasts were lactating. The heart was essentially normal. There were a few rales in the bases of the lungs. The lower quadrants of the abdomen were spastic and tender. The uterus was in the midline, extended half the distance to the umbilicus and was very tender. Bilateral costovertebral tenderness was present.

A Wassermann test was negative. The blood showed a white-cell count of 14,800 and the urine contained many pus cells. A blood culture showed the presence of *Staphylococcus albus*.

The treatment was essentially conservative. The patient was given rectal fluids, the bladder was irrigated, and hot douches were administered. Her condition became progressively worse, and on the day following entry she was irrational. She died on July 21, one week after admission.

Comment. This is another case of a normal delivery which resulted in fatal puerperal sepsis. It is possible that in spite of the history there was fever before the tenth day. In cases in which the infection does not begin until the tenth day a fatal outcome is most unusual, except for those involved in a hospital epidemic, when the infection may start almost any time during convalescence.

The uterus was left entirely alone, but in spite of conservatism, the infection was overwhelming. Whether or not *Staphylococcus albus* was the etiologic agent was unproved; its recovery from a blood culture usually indicates contamination. The efficacy of the douches is open to question. They may do some good in low-grade parametric infections, but there can be no rationale for their use in cases of general sepsis.

DEATHS

CRANDON — Le Roi G. Crandon, M.D., of Boston, died December 27. He was in his sixty-seventh year.

Born in Chelsea, he attended the Chelsea High School and Harvard University. He received his degree from the Harvard Medical School in 1898. Dr. Crandon was a house officer at the Boston City Hospital for two years and then began the practice of surgery. He was visiting surgeon at the Boston City Hospital from 1903 to 1918, assistant in surgery at the Harvard Medical School from 1904 to 1917 and secretary of the Suffolk District Medical Society from 1903 to 1908.

In 1917 Dr. Crandon organized Naval Station Hospital Unit No. 9 and entered the navy with the rank of lieutenant-commander, serving until 1919.

Dr. Crandon was a fellow of the Massachusetts Medical Society, the American Medical Association and the American College of Surgeons.

His widow survives him.

HALL — Josiah N. Hall, M.D., of Denver, Colorado, died December 20. He was in his eighty-first year.

Born in North Chelsea, he received his degree from Harvard Medical School in 1882. Before moving to Colorado he served as house physician at the Boston City Hospital for eighteen months. He practiced in Colorado for fifty-four years. At the time of his death he was professor of medicine, emeritus, at the University of Colorado School of Medicine. He was also a past president of the Colorado State Board of Medical Examiners and the Colorado State Board of Health, and had served as a physician for the city and county of Denver.

Dr. Hall was a former member of the Massachusetts Medical Society and was a fellow of the American Medical Association, the American College of Physicians and the American Clinical and Climatological Association.

JACOBS — Henry B. Jacobs, M.D., of Baltimore, Maryland, died December 20. He was in his eighty-second year.

Dr. Jacobs was born in Scituate and attended Harvard University. He received his degree from Harvard Medical School in 1887 and interned at the Massachusetts General Hospital. He joined the staff of the Johns Hopkins Hospital in Baltimore, where he became an authority on tuberculosis.

Dr. Jacobs was a former member of the Massachusetts Medical Society and was a fellow of the American Medical Association.

CORRESPONDENCE

SUGGESTION FOR A NEW COMMITTEE

To the Editor: The communication published in the December 7 issue of the *Journal* from Medical and Surgical Associates, suggests the possible development in Massachusetts of prepaid medical care furnished by group medical practice. It is to be expected that after and possibly during an experimental period, should this method appear to the public sound and desirable, such groups will multiply and render service in a variety of ways.

If and when such types of contract medicine increase and multiply, the greatest danger — both to the public and to the profession — will be from inadequate personnel and poor service. In the past, some forms of contract medicine have resulted in a deterioration of medical service. It is of interest to organized medicine and to the public that this should not happen in the future. In helping to avoid this danger and at the same time in permitting experimental solution of the economic and medical problems involved, lies a great opportunity of organized medicine to be of service to the public. Within organized medicine is to be found the only group of experts who can properly appraise the quality of medical care provided by group medical practice and effectively pass judgment on such practice for the purpose of maintaining and improving the standards of medical care.

I therefore suggest that the Massachusetts Medical Society might wisely set up a committee charged with the duty to study the quality of medical care which such groups give and to report its findings to the Society. It seems probable that it would be wise to set up for this purpose a new committee, since the work might well become burdensome and be somewhat different from that of any of the present existing committees. This committee should be composed of men steeped in the wisdoms of clinical medicine, but it might also wisely include physicians primarily concerned with the fundamental sciences and with hospital administration.

Such a committee representing the Massachusetts Medical Society, which has long held a high position in the public regard, might have a tremendous influence not only in collecting facts upon which the official opinions of the Society might be based, but in influencing public opinion through which, in the last analysis, the medical profession can most certainly influence social changes.

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As an introduction two cases of jaundice were presented. The first of these was that of a forty-nine-year-old man who had showed almost complete lack of bile pigments in the stools since the beginning of his jaundice three weeks before entry. The diagnosis had not been definitely established but lay between catarrhal jaundice and pancreatic carcinoma. The second case was that of a thirty-nine-year-old woman who had had a cholecystectomy for stones in May, 1939. At that time the common duct was explored and said to be normal; fifteen days postoperatively bile had drained through the wound. Since operation she had had several attacks of pain in the right upper quadrant, one of which was associated with jaundice and itching. The diagnosis on this admission was thought to be common-duct stone.

Dr. Otto Schales, the principal speaker of the evening, was then introduced. His topic was "Pseudohemoglobin and Related Compounds in Health and Disease."

After a few preliminary remarks on the structure and chemical reactions of hemoglobin and an enumeration of other iron-containing physiological substances, Dr. Schales discussed the properties of pseudohemoglobin.

When normal blood is treated with dilute hydrochloric acid, ionized iron is liberated in constant amounts (about 15 mg. per liter of blood). It has been shown that this iron is not derived from hemoglobin but from related compounds, "E" and "E_1" which occur in the red-blood cells.

It has been shown that compound "E" reacts with carbon monoxide and that its relative carbon monoxide affinity is about ten times greater than that of hemoglobin. In combination with carbon monoxide, compound "E" will not liberate ionized iron when treated with dilute hydrochloric acid. This fact has been utilized in testing for low concentrations of carbon monoxide in the blood, since the carbon monoxide combines first with compound "E" and later with hemoglobin. Even when spectroscopic examination of a blood suspected of containing carbon monoxide fails to reveal the presence of carboxyhemoglobin, treatment of the blood with dilute hydrochloric acid will fail to release ferrous ion in normal amounts when even very small quantities of the gas are present. As the patient recovers from his exposure to the gas, the ionized iron obtainable rises to a normal value.

Chemical studies have shown that compound "E" contains a pseudohemin in which the porphyrin ring, which is closed in hemoglobin, is open. Compound "E" has been called alpha-pseudohemoglobin to denote this relation. Alpha-pseudohemoglobin will react with carbon monoxide as related above, but not with cyanides. It can be converted to a related compound in which the iron contained within the molecule is in the ferric state — a substance analogous to methemoglobin — and which normally represents about one third of the "easily split off" iron in blood. This substance is known as alpha-pseudomethemoglobin or compound "E_1"; it reacts with cyanides but not with carbon monoxide. The other reactions of alpha-pseudohemoglobin and alpha-pseudomethemoglobin are similar to their related compounds, hemoglobin and methemoglobin, with which they are identical so far as the protein (globin) as bearer of the prosthetic groups is concerned.

Hemoglobin may be converted into alpha-pseudohemoglobin by means of hydrogen peroxide in presence of potassium cyanide and also by certain reducing agents in presence of oxygen. Perhaps the ascorbic acid in the blood, acting by producing nascent hydrogen peroxide, is responsible for the normal breakdown of hemoglobin into bile pigment by this route, with pseudohemoglobin and pseudomethemoglobin as intermediate products of bilirubin formation. Since hydrogen sulfide produces hydrogen peroxide in the presence of oxygen, sulfhemoglobin may be closely related to the pseudohemoglobins.

Little is known about the blood level of pseudohemoglobins in pathologic conditions. It is about half normal in pregnancy, carcinomatosis and habitual tobacco smokers. It is three-quarters normal in cases of general paresis following malaria treatment and less than half normal in lead poisoning. These values are independent of the blood hemoglobin levels.

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Dr. E. J. Cohn in discussing the paper suggested that the study of pseudohemoglobins might be of great im-

portance because changes related to them appear before changes related to hemoglobin and in spite of compensatory mechanisms which keep hemoglobin normal.

Dr. Arnold P. Meiklejohn pointed out the fact that the previous theory was that hemoglobin was broken down normally by conversion into porphyrin. If it is true that hemoglobin is converted normally into pseudohemoglobin by breakage of the porphyrin ring, then the presence of porphyrin in the urine takes on a pathological significance hitherto unappreciated.

NOTICES

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Case Reports:
Femoral embolectomy.
Habitual abortion.
Subacute bacterial endocarditis.

Physicians and medical students are cordially invited to attend.

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All those interested in the subject are cordially invited to attend.

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and Cornell University Medical College. The fellowship will be available on July 1 at the beginning of the academic year. Applications for the year 1940–41 should be in the hands of the committee by February 15. It is expected that the award will be made by April 1.

Application for this fellowship should be addressed to: Committee of the Lewis Cass Ledyard, Jr., Fellowship, The Society of The New York Hospital, 525 East 68th Street, New York City.

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Monday, January 15

Monday, January 15

*11:30 a.m. Monthly clinical meeting. Carney Hospital.

*12:15–1:15 p.m. Clinicopathological conference. Dr. S. Burt Wolbach, Peter Bent Brigham Hospital amphitheater.

*5 p.m. Cutter Lecture. Harvard Medical School, Amphitheater E.

*8:15 p.m. Boston Medical History Club. Boston Medical Library, 8 Fenway.

Tuesday, January 16

*9–10 a.m. Nephritic Clinic. Presentation of cases. Dr. R. W. Buck. Joseph H. Pratt Diagnostic Hospital.

*10 a.m.–12:30 p.m. Boston Dispensary tumor clinic.

12 m. South End Medical Club. Headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston.

*12:15–1:15 p.m. X-ray conference. Dr. Merrill C. Sosman. Peter Bent Brigham Hospital amphitheater.

Wednesday, January 17

*9–10 a.m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*12 m. Clinicopathological conference. Children's Hospital amphitheater.

*2–4 p.m. Joint medical and surgical clinic. Peter Bent Brigham Hospital.

Thursday, January 18

*8:30–9:30 a.m. Combined clinic of the medical, surgical, orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital, at the Children's Hospital.

*9–10 a.m. Surgical case: clinicopathological presentation. Dr. H. F. Day. Joseph H. Pratt Diagnostic Hospital.

11 a.m. Tumors of the Pituitary Body. Dr. Oscar Hirsch. Boston City Hospital.

Friday, January 19

*9–10 a.m. A Discussion of Rheumatic Fever. Dr. T. Duckett Jones. Joseph H. Pratt Diagnostic Hospital.

*10 a.m.–12:30 p.m. Boston Dispensary tumor clinic.

*12 m. Urological conference at the Massachusetts General Hospital, lower amphitheater, Out-Patient Department.

*12 m. Clinical meeting of the Children's Medical Service, Massachusetts General Hospital. Ether Dome.

Saturday, January 20

*9–10 a.m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*10 a.m.–12 m. Medical staff rounds of the Peter Bent Brigham Hospital. Conducted by Dr. Soma Weiss.

Sunday, January 21

4 p.m. What about Sulfanilamide? Dr. Chester S. Keefer. Free public lecture. Harvard Medical School, amphitheater of Building D.

*Open to the medical profession.

January 12 — United States Marine Hospital. Page 1043, issue of December 28.

January 14 — Free public lecture. Harvard Medical School. Page 1042, issue of December 28.

January 14 — Salem Hospital public lecture. Page 1042, issue of December 28.

January 14–March 10 — Free public lectures. Quincy City Hospital. Page 77.

January 15 and 16 — Second Annual Congress on Industrial Health. Page 39, issue of January 4.

January 15 and 22 — Cutter Lectures. Page 1042, issue of December 28.

January 15 — Boston Medical History Club. Page 77.

January 15 — Monthly clinical meeting. Carney Hospital. Page 77.

January 16 — South End Medical Club. Page 38, issue of January 4.

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January 18 — Combined clinic of the medical, surgical, orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital. Page 77.

January 19 — Staff meeting. United States Marine Hospital. Page 39, issue of January 4.

January 22–25 — American Academy of Orthopaedic Surgeons. Hotel Statler, Boston.

January 23 — Boston Lying-in Hospital. Page 77.

January 24 — New England Society of Physical Medicine. Hotel Kenmore, Boston.

February 8 — Pentucket Association of Physicians. 8:30 p.m., Hotel Bartlett, Haverhill.

February 11–14 — International College of Surgeons. Page 759, issue of November 9.

February 22–24 — American Orthopsychiatric Association. Page 957, issue of December 14.

March 2, June 8 and 10 — American Board of Ophthalmology. Page 719, issue of November 2.

March 7–9 — The New England Hospital Association. Hotel Statler, Boston.

April 24–26 — Scientific Session. Academy of Physical Medicine. Hotel John Marshall, Richmond, Virginia.

May 10–18 — American Scientific Congress. Page 1043, issue of December 28.

May 14 — Pharmacopoeial Convention. Page 894, issue of May 25.

June 7–9 — American Board of Obstetrics and Gynecology. Page 1019, issue of June 15.

District Medical Societies

ESSEX SOUTH

February 14 — Cough, Sputum, Hemoptysis — How shall they be investigated? Dr. Reeve H. Betts. Essex Sanatorium, Middleton.

March 6 — Experimental and Clinical Considerations of Sulfanilamide Treatment of Hemolytic Streptococcal Infections. Dr. Champ Lyons. Lynn Hospital, Lynn.

April 3 — Addison Gilbert Hospital, Gloucester.

May 8 — Annual meeting. Salem Country Club, Peabody.

HAMPDEN

January 23 — Page 77.

HAMPSHIRE

March 13.

May 8.

Meetings are held at 11:30 a.m. at the Cooley Dickinson Hospital, Northampton.

MIDDLESEX EAST

March 20.

May 15.

Meetings are held at 12:15 p.m. at the Unicorn Country Club, Stoneham.

MIDDLESEX NORTH

January 31.

April 24.

July 31.

October 30.

NORFOLK

January 30 — Page 77.

NORFOLK SOUTH

February 1.

March 7.

April 4.

May 2.

All meetings, with the exception of one which is usually held at the Quincy City Hospital, are held at the Norfolk County Hospital in South Braintree, at 12 o'clock noon.

PLYMOUTH

January 18 — Brockton Hospital, Brockton.

March 21 — Goddard Hospital, Brockton.

April 18 — State Farm.

May 16 — Lakeville Sanatorium, Lakeville.

SUFFOLK

January 31 — Scientific meeting. Subject to be announced later.

March 27 — Scientific meeting. Symposium on Ulcerative Colitis and Diarrheas. Under the direction of Dr. Chester M. Jones.

April 24 — Annual meeting in conjunction with the Boston Medical Library. Election of officers. Program and speakers to be announced later.

WORCESTER

February 14 — Worcester State Hospital

March 13 — Worcester Memorial Hospital.

April 10 — Worcester Hahnemann Hospital.

May 8 — Worcester Country Club.

Each meeting begins with a dinner at 6:30 p.m. and is followed by a business and scientific meeting.